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Archives of Dermatology and Syphilology

VOLUME 13 FEBRUARY, 1926 NUMBER 2

CREEPING ERUPTION *

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This paper is a preliminary report of studies on "creeping eruption," a disease which has generally been considered as being a myiasis. Five microscopic nematode parasites have been recovered from serial sections of skin tissue excised from patients with creeping eruption at Jacksonville, Florida. These were taken from patients having multiple lesions. This is the first recovery of this nematode from lesions of creeping eruption.

The findings of Samson [1] and Sokolow [1] in which they recovered larvae identified as *Gastrophilus* by Cholodowsky [1] and the subsequent reports by others (Table 1) have given the impression that *Gastrophilus* and other fly larvae are the exciting causes of creeping eruption. As the majority of workers have failed to find a larva, and as the senior author [2] (J. L. K-S) could not correlate the geographic distribution of *Gastrophilus* with the occurrence of the disease in Florida, an insistent request was made to Mr. F. C. Bishopp of the Bureau of Entomology, for entomologic assistance. Accordingly, Dove was directed to assist while conducting other work in that vicinity. He observed at least 300 cases and studied the conditions under which they had developed. From these numerous skin excisions were made. Many of them were sectioned serially. This was done under the supervision of White and studied by him or under his direction.

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* From the United States Bureau of Entomology.

* Published by permisson of the Chief of Bureau of Entomology.

* Read before the section on Dermatology and Syphilology, at the Seventy-Sixth Annual Session of the American Medical Association, Atlantic City, N. J., May, 1925.

1. Tamura, H.: On Creeping Disease, British J. Dermat. & Syph. **33**:81-102, 138-151 (March) 1921.

2. Kirby-Smith, J. L.: Creeping Eruption, J. Florida M. A. **4**:95-100, 1917.

HISTORY AND DISTRIBUTION

In 1874, Lee [3] described a case of "creeping eruption," and in 1884 he [4] reported a second case. In 1892, Crocker [1] reported another case from England under the caption "larva migrans," and indicated that the disease occurred also in Arabia. Later writers (Table 1) give its occurrence as in Ireland, Scotland, the Shetland Islands, Norway, Sweden, Denmark, Russia and Siberia, Bulgaria, Arabia, Sumatra, China, Japan, Germany, Austria, France, Switzerland, Siam, the United States, Brazil and West Africa (Senegal, Sierra Leone, Liberia, Togoland, Nigeria and the Cameroons). From the literature it would seem that the disease is more prevalent in eastern Russia, where children are found to be more often infected.

In 1902, Van Harlingen [5] reported a case in the United States. In 1903, Stelwagon [1] reported a case, and in 1904, he [6] mentions a case seen by Dr. Green, Elmira, N. Y., in 1901. Since that time reports have been made from the southern and eastern coasts of the United States.

CAUSATION BY FLY LARVAE

Gastrophilus myiasis.—The reports of Samson, Sokolow, Wosstrikow and Bogrow, Boas, Ruddell,[1] Cates [7] and Schalek [8] incriminate *Gastrophilus* as a causative parasite of creeping eruption. These are supported by authentic identifications or by photographs of the parasite. Rille and Riecke [9] review such infestations.

It is interesting to note that in all the foregoing cases, infection occurred on the neck, face, arms or other parts not covered by clothing. Samson [1] describes an itching pain, but in none of the other reports on *Gastrophilus* has any reference regarding pain been found. Professor Boas' patient had a bright red, raised, wavy line about 1 mm. in width extending from an excoriation covered with a crust. On the third day the area at the extremity of the line became edematous. On either side there was a white, slightly raised, edematous border, making the entire breadth of the lesion about 2 mm. Wosstrikow and Bogrow described

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3. Lee, R. J.: Case of Creeping Eruption, Tr. Clin. Soc. Lond. **8**:44-45 (Nov.) 1874.

4. Lee, R. J.: Short Notice of a Second Case of Creeping Eruption, Etc., Tr. Clin. Soc. Lond. **17**:75-76 (Jan.) 1884.

5. Van Harlingen, A.: Report of Three Cases of Creeping Larvae in the Human Skin (Hyponomederma Kaposi), Am. J. Med. Sc. **124**:436-441, 1902.

6. Stelwagon, H. W.: A Second Case of Creeping Eruption, J. Cutan. Dis. **22**:359-362, 1904.

7. Cates, T. H.: Creeping Eruption, Dermat. Wchnschr. **58**:417 (April 11) 1914.

8. Schalek, A.: Report of First Case of Creeping Disease in Nebraska, Nebraska M. J. **8**:38-39 (Jan.) 1924.

9. Rille, J. H., and Riecke, E.: Creeping Disease, Mraček Handbuch der Hautkrankheiten, Wien., Alfred Hölder, 1905, p. 178-236.

a raised, ridgelike line from 3 to 4 mm. wide extending in a clublike ending. The base of the ridge was pearly and yellowish with narrow borders of a rose color.

Dr. Schalek [8] says that the parasite tunnels very superficially through the epidermis. His specimen was kindly loaned to us and was identified as *Gastrophilus haemorrhoidalis*.

Such cases are described as often being characterized by a linear lesion terminating with a black dot, the lesions usually being one or two in number and often having an itching sensation with little indication of pain.

Hypoderma myiasis.—In 1910, Miller [10] and, in 1889, Kane [11] gave similar descriptions of the migration of *Hypoderma*, although the former was dealing with *H. lineatum* and the latter with *H. bovis*. In each case the advancing end was characterized by a small lump changing irregularly in position and having in general an upward course.

In 1901, Topsant [1] recovered a larva which was determined by Professor Blanchard as a second stage of *Hypoderma lineatum*. According to Topsant, the invasion began at the lower part of the neck and passed over the right shoulder, making a course 64 cm. in length. The parasite was extracted from a swelling behind the neck as large as a hazelnut. The skin over the course of the larva was red and was raised slightly at unequal intervals. Sometimes its trace was lost and then again appeared. The condition was characterized by extreme pain like pin pricking, causing fits of fainting every two or three hours.

In Miller's case there was a tenderness and a stinging sensation that was more pronounced at night, but no extreme pain. At times the lump would increase to the size of two fists and become very painful.

Other Fly Larva Infestations.—According to some reports (Table 1), macroscopic larvae were recovered from creeping eruption lesions but unfortunately not identified. Whether they were causative of the disease or secondary invaders we are unable to say. Such reports serve to emphasize the importance of submitting specimens for an authentic determination of the species.

It seems well to call attention to Dr. Walker's case of dermal myiasis from which larvae were reared on raw beef and determined as *Wohlfahrtia vigil*. This type of human myiasis is not a creeping kind. In every instance the larvae were removed from boil-like sores occurring in an infant. In 1923, the same species of fly was recorded by Shannon [12] from young rabbits and a young pup in which the maggots had

10. Miller, R. T.: Myiasis Dermatosa Due to the Ox Warble Flies, J. A. M. A. **55**:1978-1979 (Dec. 3) 1910.

11. Kane, E. R.: A Grub Supposed to Have Traveled in Human Body, Insect Life **2**:238-239, 1889.

12. Shannon, R. C.: Non-Human Host Records of *Wohlfahrtia*, Proc. Ent. Soc. Wash. **30**:142, 1923.

worked their way deep into the flesh, leaving the host as mature larvae about four days afterward. This fly apparently has a preference for infants and newly born animals. It seems probable that the cases in infants reported by Spoor [13] in 1907 and by Foster [14] in 1903 were caused by this species.

CAUSATION BY NEMATODES

Gnathostomiasis.—In 1909, Professor Leiper [15] reported that the natives of Siam are occasionally affected by subcutaneous tumors due to the presence of a small nematode about 1 cm. in length and 0.6 mm. in breadth, known as *Gnathostoma siamense* (Levinsen), but which he suggests may eventually prove to be *Gnathostoma spinigerum* (Owen).

In 1921, Professor Tamura [1] discussed the finding by Ikegami (1919) of a worm in a creeping disease at the extremity of a typical, erythematopapular, serpentine line, 21 cm. long. The parasite measured 2 mm. in length and had a breadth of 0.4 mm. and was called *Echinorhynchus sphaerocephalus.*

The lesions described by Tamura indicate that his larva had turned backward, resulting in new lines extending from the old burrow. The smallest diameter observed for the new line was 1 mm., which is the diameter of the parasite recovered. This worm was identified as *Gnathostoma siamense.*

In 1924, Morishita [16] reported a pig nematode *Gnathostoma hispidium* as a human parasite. He mentions that two additional *Gnathostoma* infections in man had been encountered in China, and says that at least four cases have previously been reported and identified as *Gnathostoma spinigerum* (Owen). According to him, the geographic distribution of *Gnathostoma* from human cases is restricted to Siam, the Malay States, China and Japan. In 1925, Morishita and Faust [17] discussed the occurrence of gnathostomiasis in Eastern Asia.

Another Nematode Infection.—We are studying another nematode infection occurring in the southeastern and southern coastal areas of the United States. It is of this disease that the senior author has observed more than 2,500 cases during the fifteen years of his practice at Jacksonville. It has been seen also in the Carolinas, Georgia, Ala-

13. Spoor, A. A.: Infection with Fly Larvae, J. A. M. A. **49**:1775 (Nov. 23) 1907.

14. Foster, Burnside: *Gastrophilus epilepsalis* Larvae in the Skin of an Infant, Clinical Notes, St. Paul M. J. **5**:772-773, 1903.

15. Leiper, R. T.: The Structure and Relationships of *Gnathostoma siamense* (Levinsen), J. Parasitology **2**:77-80, 1909.

16. Morishita, K. O. R.: A Pig Nematode, *Gnathostoma hispidium* Fedshenko, as a Human Parasite, J. Parasitology **18**:23-26 (Jan.) 1924.

17. Morishita, K. O. R., and Faust, E. C.: Two New Cases of Human Creeping Disease (Gnathostomiasis) in China, J. Parasitology **9**:159-162 (March) 1925.

bama, Texas and Oklahoma. The cause of this disease is a larval nematode. This we are reporting in the present paper.

THE NAME "CREEPING ERUPTION"

From the foregoing discussion it will be observed that the name "creeping eruption" has been used for a number of different diseases. Lee [3] was among the first to use it for a human disease having a linear skin eruption with an advancing end believed to be caused by a migrating parasite. The causal organism was searched for but not found. A similar disease was also encountered in England by Crocker.[1] He, too, did not find a parasite, but believed it to be an insect larva, and reported the case under the caption "larva migrans." It is not possible to know definitely whether the two cases seen by Lee are the same condition as that in the one seen by Crocker. Neither is it possible to know whether the disease that we are discussing in the present paper is the one encountered by Lee or Crocker. Among the various other names which have since been introduced are the following: hyponomoderma, creeping disease, dermomyiasis, linearis migrans oestrosa, epidermitis linearis migrans.

It will be noted that among these creeping diseases there is a group due to the invasion of the skin by insect larvae, and that there is a second group due to invasion by nematode larvae of the genus *Gnathostoma*. There is still a third disease reported in the present paper which is due to another and very different nematode.

Names for the different creeping diseases are needed. The senior author has been using the name "creeping eruption" in his practice and in his writings for a disease having a linear, tortuous and serpiginous eruption. It is this disease for which we suggest the name "creeping eruption," leaving it to those working on the other creeping diseases to choose suitable names for them.

SYMPTOMS

Creeping eruption is characterized by a linear, tortuous, and serpiginous eruption (Figs. 1, 2, 11, 12, 13, 14, 15, 16 and 17) caused by the migration of a nematode parasite within the skin and accompanied by intense itching. The most recent visible lesion is a very narrow erythematous formation along the course traversed by the worm. Soon a slightly raised line representing the location of the burrow can be palpated. This line becomes visibly elevated, more or less continuous and vesicular (Figs. 2 and 12). Sometimes bullae are formed (Fig. 3, *C*, *E* and *F*). The surface of the lesion dries, resulting in a thin crust. When the parasite travels it moves from a fraction of an inch to several inches a day, advancing, as a rule, more rapidly at night.

Following the penetration of the skin the parasite apparently remains at the point of entry before migrating, resulting in a reddish, sensitive

Fig. 1.—Extensive creeping eruption infections: *A*, Case 239, a blacksmith, not secondarily infected through scratching; *C*, Case 165, a plumber, infected through scratching, duration sixteen days; *B* shows papular eruption, duration two days, at points of ingress of the nematode larvae, *Agamonematodum migrans*.

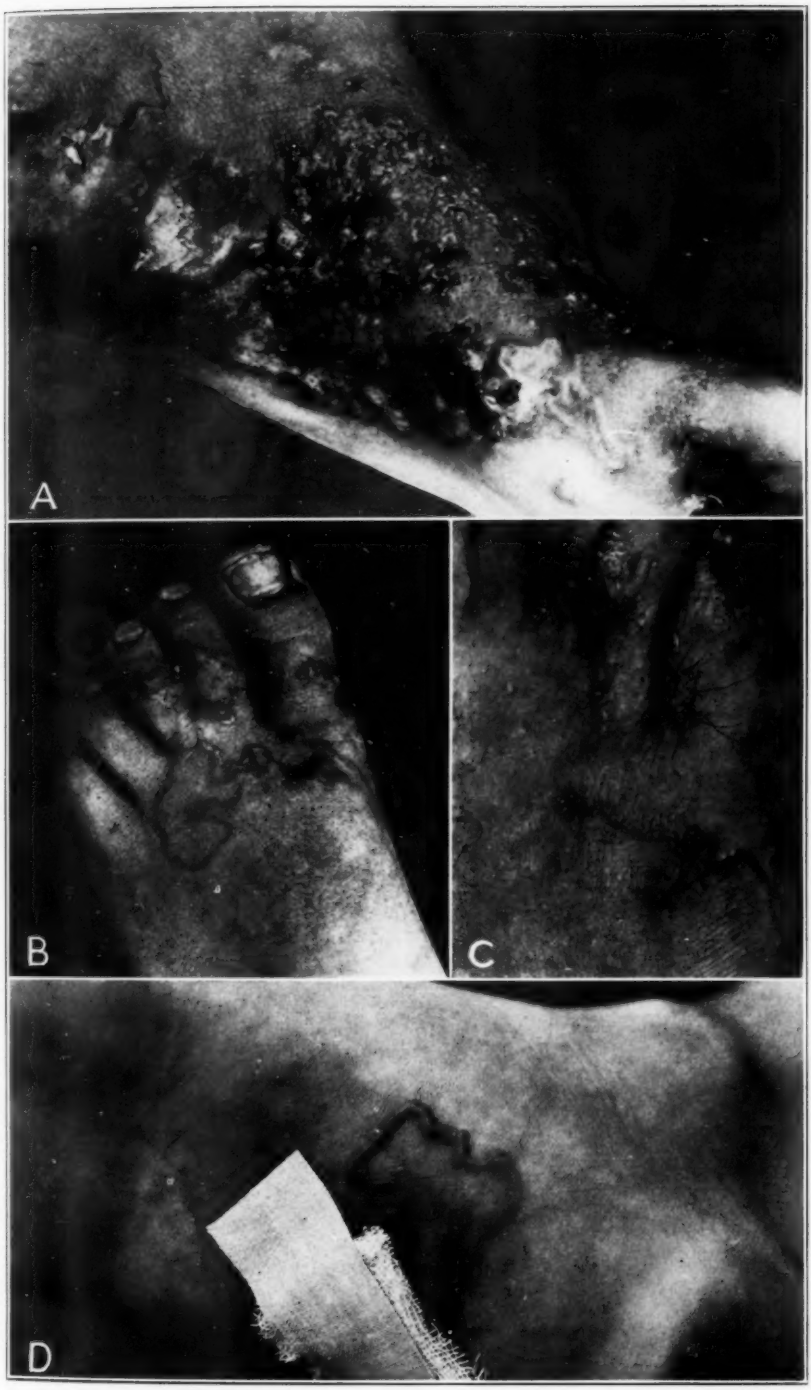

Fig. 2.—Lesions of creeping eruption on the feet: *A*, ruptured through scratching and secondarily infected; *B* and *C*, lesions as often encountered; *D*, migration after unsuccessful attempt to recover larva by excision.

papule not unlike that of the bites of "chiggers," "red bugs" or "harvest mites" (Fig. 1, *B*). From these points the advancing threadlike burrows may be observed within from two to four days. The raised portion of the skin over the burrow has the appearance of that made by a mole in meadows and elsewhere (Fig. 2). The end most distant from the parasite may be 0.5 cm. in width and may sometimes give the lesion a tapering appearance. Abrupt changes in the direction of the burrow are frequently observed. The migration has been observed on a number of occasions to have continued for several weeks, and some observations indicate that the larva had migrated for months. In such cases the travel of the larva is interrupted by periods of rest. Often the scratching results in bacterial infections and raw surfaces (Fig. 1, *C;* Fig. 2, *A;* Fig. 15).

In his practice the senior author has observed lesions on every part of the body. Since infections take place on those portions coming in contact with the soil, the lesions occur most often on the feet (Fig. 2). The buttocks and hands (Fig. 2, *A;* Fig. 17 *A*) also frequently become infected.

At the time of ingress of the parasite the sensation experienced may be compared to the bites of mosquitoes or ants or to contact with nettles. Itching follows and becomes so intense as to be almost unbearable. Loss of sleep and appetite occurs and in extreme cases loss of weight and vitality.

METHODS OF ATTACK

The object of the present studies has been to determine the cause of creeping eruption and the various factors affecting the occurrence of the disease and to improve the treatment. The literature, together with the seasonal incidence of the disease indicated that in all probability the problem was an entomologic one. Kumberg (1898), Schmidt (1900), Wosstrikow and Bogrow (1908), Cates[7] (1910), Rudell (1913), Knowles[18] (1916), and Kirby-Smith[2] (1918) had recovered larvae from lesions of creeping eruption, but the identity of these was not established.

A clinic of ten days was started at Jacksonville, on July 21, 1924, to which due publicity was given. This was supported by members of the medical profession, and splendid cooperation was received from the Florida State Board of Health and the Jacksonville City Board of Health. At this clinic, 179 cases of creeping eruption were observed, and during the summer a total number of 300 were seen.

From the various locations of the origin of infections, samples of soil were obtained and sealed in glass jars. The tops of these were fitted with glass vials anchored with adhesive tape, and were exposed

18. Knowles, F. C.: Creeping Eruption, J. A. M. A. **66**:172-177 (Jan. 15) 1916.

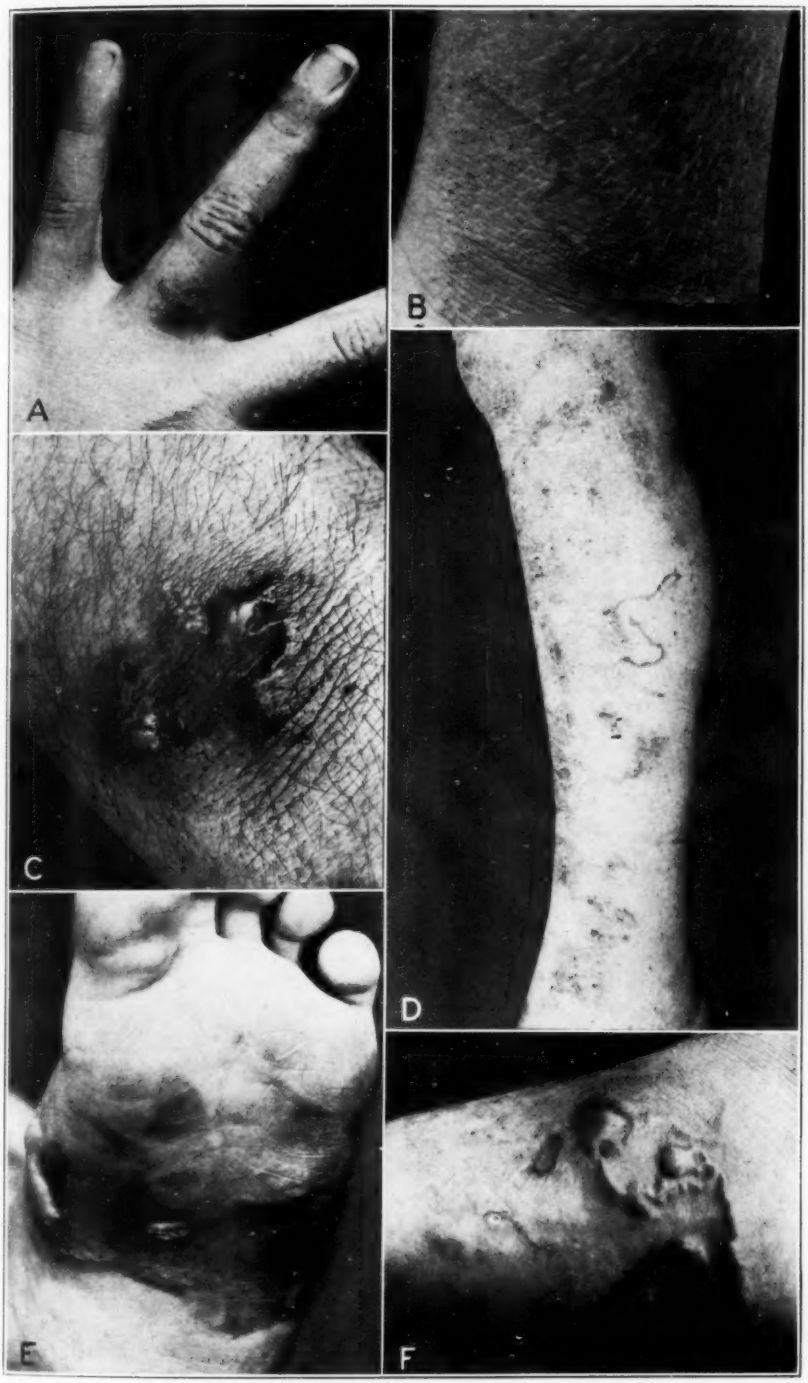

Fig. 3.—Creeping eruption on extremities: *A*, lesion on ring finger; *B*, linear lesion on dorsum of wrist; *C*, bulla on forearm; *D*, few remaining active lesions on leg following treatment; *E*, close-up view of lesion on foot showing infiltration and bullae; *F*, migration across plantar surface of foot, with bulla and infiltration.

to the light so that any flies emerging would be attracted into the tubes. These were carefully examined at frequent intervals with a dissecting binocular microscope. Only occasionally could a fly be reared, and then it was of such a nature that it was not considered as causative by Dove or Bishopp. When such soil was collected for rearing flies, waste scraps and fly breeding mediums were seldom found in quantities sufficient to rear them. The use of well covered garbage cans and the prompt disposal of garbage by the city, practically kept fly breeding under control.

Detailed information was obtained from the patients regarding points bearing on the epidemiology of the disease. The homes of infants and invalids were especially studied, as it was physically impossible that such persons could have visited locations without some recollection of such visits.

Studies of the sanitation, probable transmission of the disease and possible host relationships of the parasite were made during this survey, and experimental animals, including man, were exposed in such locations for possible infection.

Excisions were made from the terminals of lesions of patients when their locations would permit. To include the larva in the excised skin it was necessary to remove an area beyond the visible lesion of the migrating parasite. On account of the varying speed at which the worm travels it was impossible definitely to determine its location. More than 200 pieces of skin tissue were removed, and of these forty-eight were completely sectioned serially, making more than 40,000 sections for study.

ETIOLOGY

Fly Larvae.—Gastrophilus was not observed during the study at Jacksonville, but it occurs in some portions of the state. Dove [19] made biologic studies on this group of horse infesting flies in South Dakota, where they are sufficiently abundant to be a serious pest. Creeping eruption in man has never been reported from that state. At Jacksonville, there were no indications that this genus of flies could be concerned in the causation of the disease.

Hypoderma which infest cattle and which normally make their ingress into the host by burrowing [20] do not occur in the southern portion of Florida and are of rare occurrence at Jacksonville. While it would be possible for a case of creeping eruption to be caused by larvae of

19. Dove, W. E.: Some Biological and Control Studies of *Gastrophilus haemorrhoidalis* and Other Bots of Horses, U. S. Dept. Agr. Bull. 597, April, 1917.

20. Bishopp, F. C.; Laake, E. W.; Brundrett, H. M., and Wells, R. W.: The Cattle Grubs or Ox Warbles; Their Biologies and Suggestions for Control, U. S. Dept. of Agr. Bull. **20**, November, 1925.

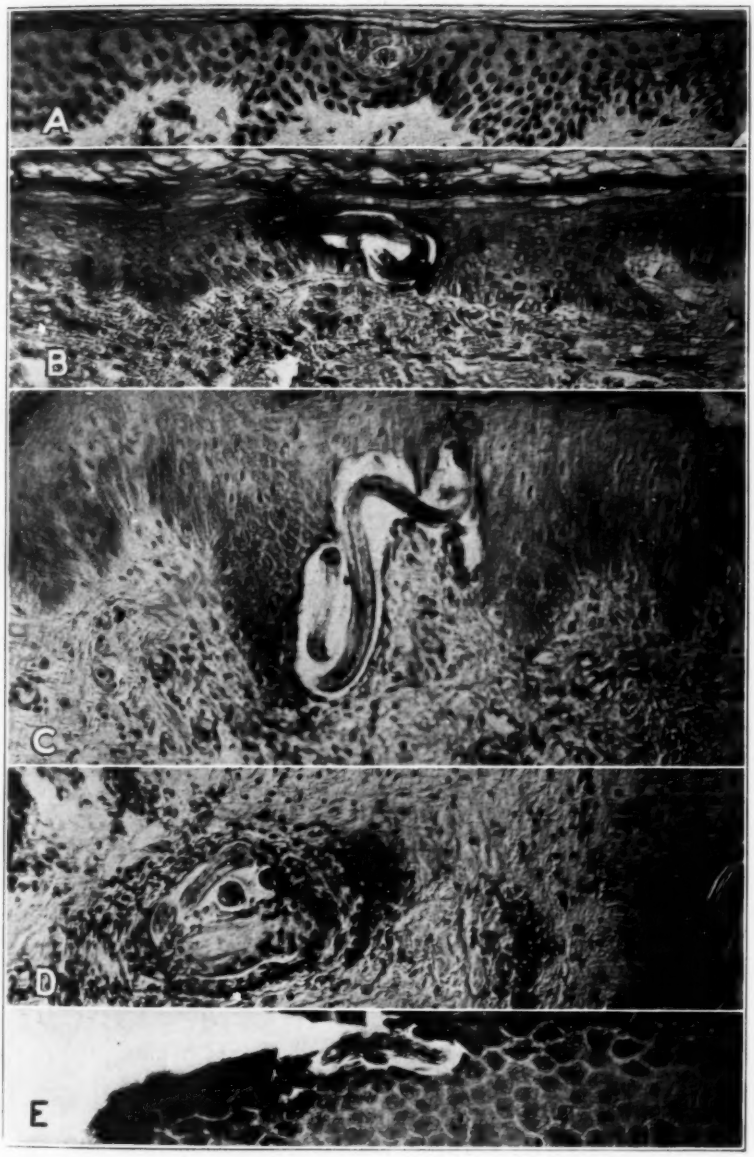

Fig. 4.—Photomicrographs of five larvae of Agamonematodum migrans; magnification × 190. *A*, Case 165, cross section of larva, the burrow containing many other cellular elements; *B*, also Case 165, larva partially coiled in burrow and located in stratum mucosum; *C*, Case 199, lies partly coiled in burrow near sweat duct; *D*, Case 232, parasite lies coiled in outer sheath of hair follicle, about 0.5 mm. from surface of the skin; *E*, worm lies within the granular layer of the epidermis.

this fly, it is highly improbable that any cases are caused by them in the locality of Jacksonville.

The appearance of lesions in tapering to a faint line on the advancing end indicated that the causative larva was practically microscopic. Some of these lines terminate in a nodule and are large enough to suggest the presence of a larva the size of those of certain meat-infesting flies. In examinations of these nodules no larvae were observed at Jacksonville during the summer of 1924.

If meat-infesting fly larvae have been encountered at any time it would seem that they were probably secondary invaders. It is important to determine what kinds of flies are capable of infesting human lesions in this manner.

The burrows of many patients were opened, and in no case was a causal parasite found. Examinations of material resulting from a blistering ointment were likewise negative. Serum drawn from areas previously frozen with carbon dioxid snow also failed to reveal the invader. Scrapings from the skin lesions of many patients were examined, both fresh and stained, and in no instance was a parasite found. Dissections of a large number of excisions under magnification were also negative.

It was not until serial microtome sections were made of excised skin that the parasite was discovered. The parasite was found to be the larval stage of a nematode. This worm was present in each of five of the forty-eight excisions sectioned, one parasite only being found to a lesion.

Histopathology.[21]—A brief description is given here of the morphologic changes that occur in the portion of the skin containing the parasite.

Case 165.—Two parasites were recovered from the patient. The tissue furnishing the first of these to be described was excised sixteen days after infection. The nematode in this instance lay extended in the burrow, the body being only slightly curved.

The burrow had the granular layer as the roof and the mucous layer as the floor and sides (Fig. 4, *A*; Fig. 5, *A*). In height it was from one to two times the diameter of the nematode and in width from two to three times. Besides the parasite, it contained swollen degenerating epithelial cells. The cytoplasm of these stained more deeply with eosin and the nuclei more intensely with hematoxylin than did the healthy cells of this layer. There was present in the burrow also many small, more or less spherical, eosin-stained bodies. Most of these at least were the granules of eosinophil cells undergoing degeneration. In it also collections of hematoxylin-stained material were found here and there.

21. Zenker's fluid, formaldehyd and alcohol were used as fixatives. Paraffin sections of 8, 10 or 12 microns were made. In staining, Harris' hematoxylin and eosin soluble in alcohol were employed in most of the work. Iron hematoxylin, Giemsa's and Van Gieson's stains were also used.

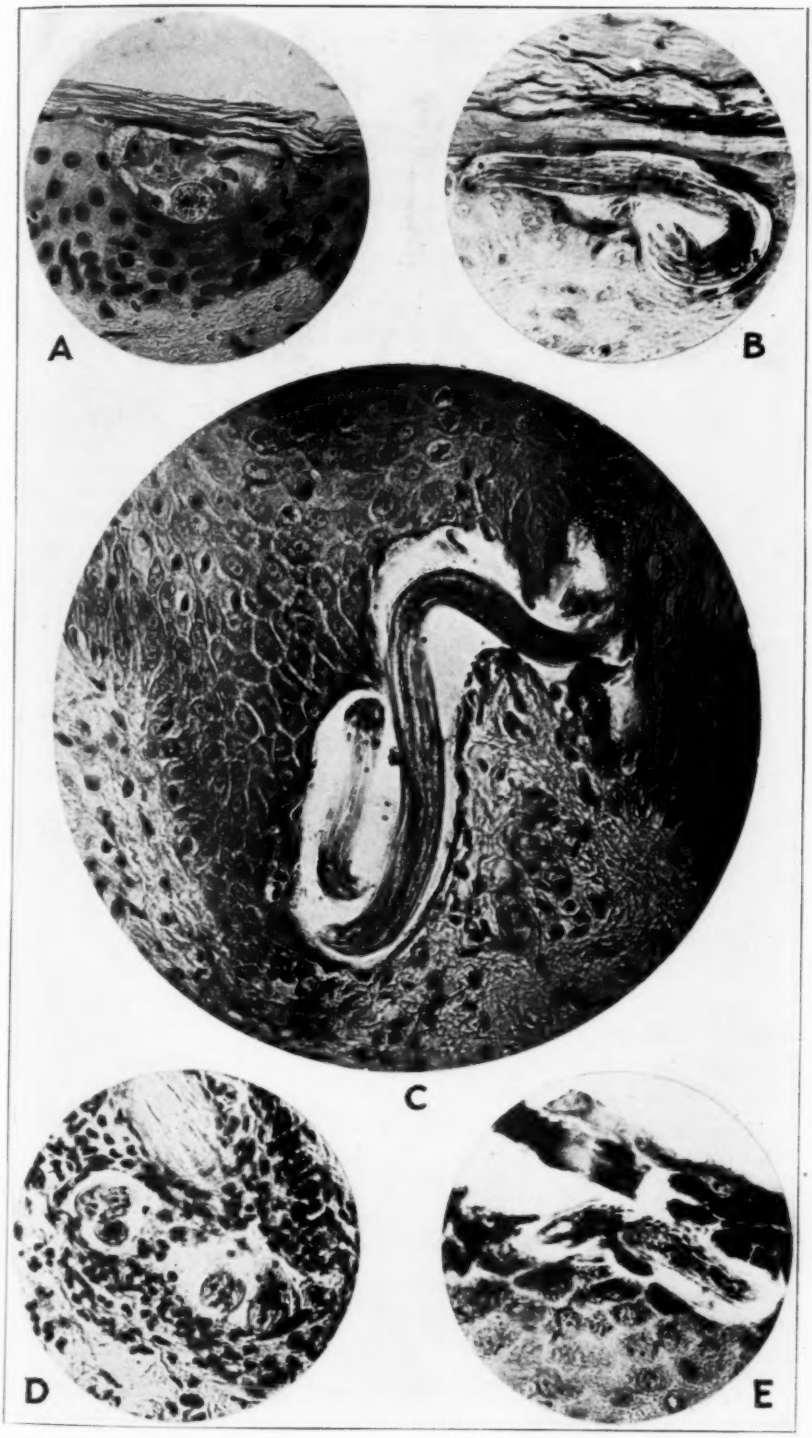

Fig. 5.—Photomicrographs of skin showing creeping eruption nematode in the burrow; × 480. Similar to Figure 4.

The observations indicated that the nuclei of the eosinophil and epithelial cells were the chief sources of this material.

The corium over the parasite was unchanged, likewise the granular layer. A few eosinophil cells occurred in the lymphatic spaces of the mucous layer. About the vessels of the corium there was a slight infiltration of round cells and there were many eosinophils. This occurred not only near the parasite but in other parts of the section as well. Eosinophils occurred also scattered in small numbers among the connective tissue bundles of this layer.

The second larva (Fig. 4, *B*; Fig. 5, *B*) recovered from the patient occurred in tissue excised nine days after infection. The worm was in a coiled position within the burrow. A complete series showed that the parasite occupied fifteen sections.

The burrow extended from the granular layer to the corium, with the mucous layer as side walls. Cellular elements besides the parasite were practically absent in the burrow. A slight cellular infiltration occurred in the corium.

The burrows and their parasites in Cases 199 (Fig. 4, *C;* Fig. 5, *C*) and 112 (Fig. 4, *E;* Fig. 5, *E*) were within the mucous layer of the skin and just beneath the granular layer. In Case 232 they were in the outer sheath of a hair follicle (Fig. 4, *D;* Fig. 5, *D*). In each of these instances the worm was more or less coiled, and the burrows were practically without other cellular elements.

That there is a hydrostatic pressure within the burrow is suggested by a number of observations: In no instance do the parasite and the other cellular elements fill it; the epithelial cells in the immediate vicinity that constitute its walls are spindle-shaped; its volume is considerably greater than the contained worm, and in somewhat older lesions its course can easily be palpated and still later be readily seen.

By way of a summary it is noted that the burrow in each of the five instances was practically within the stratum mucosum, one being in the outer sheath of a hair follicle. It may have the corium as the floor and usually has the stratum granulosum as the roof. In each instance there was evidence of a hydrostatic pressure within the burrow. In four of the five cases practically no cells of the host are within the burrow, while in the other one there are many. Two of the cases show a local eosinophilia in the tissues, three do not. Perivascular infiltration of round cells is presented to a slight degree in all instances.

When one studies the tissues along the entire course traversed by the worm, one finds other interesting changes, but they are too numerous to be described here. Infections in different persons may show morphologic differences. Still other differences may be present as a result of secondary infections, especially bacterial, and also as a result of previous local applications.

Causal Parasite.—The inciting cause of creeping eruption is the nematode larva recovered in serial microtome sections from five different excisions representing four patients and as many different localities.

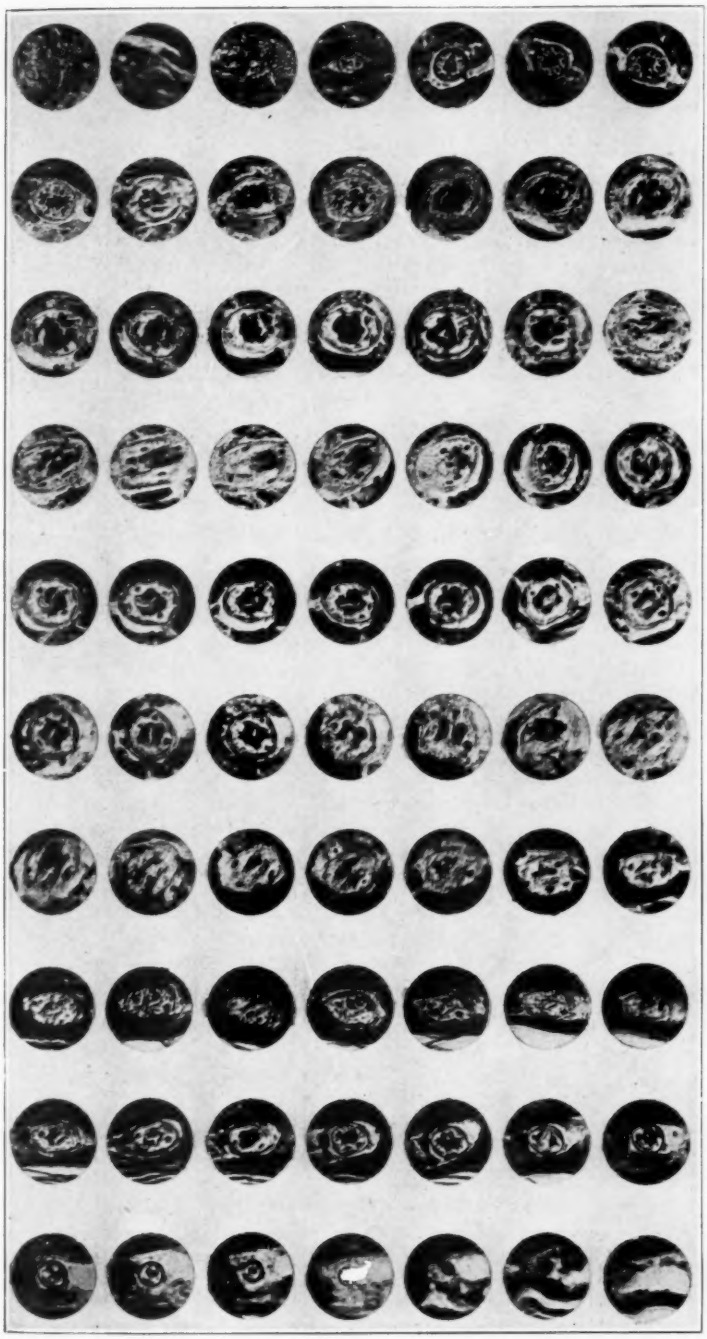

Fig. 6 (Case 165).—Entire larva in section of 8 microns mounted serially, beginning with the anterior end and reading left to right.

Agamonematodum migrans n. sp.—The larva reported in Case 165 was cut approximately in transverse sections 8 microns in thickness and occupied 68 sections, totaling, therefore, about 550 microns in length. Because of a bend in it at the time of fixation and because the general direction of the larva in the tissue was probably not such that the sections would otherwise be exactly transverse, its length probably approximates 600 microns. Its maximum breadth was 20 microns. The larva measured, therefore, somewhere between one fiftieth and one fortieth of an inch in length and about one twelve hundredth of an inch in width. The esophagus measured about two sevenths of the length of the worm (Fig. 8). The general internal structure of the larva was well revealed in the complete series of sections obtained (Fig. 6).

While the history and clinical manifestations support the position that this nematode is a new species, we are not yet certain from the observations thus far made whether it belongs to an already known species. In order to give it a designation, however, until more is known as to its identity, the name *Agamonematodum migrans* is suggested. "*Agamonematodum*" is a generic term for a collective group of immature nematodes. It is used here pending the discovery of the adult worm of the species.

Specimens of this nematode larva have been submitted to Dr. B. H. Ransom, of the Bureau of Animal Industry, for advice regarding the further classification of it, and he has kindly furnished us with the following statement:

> The nematode larvae found in cases of creeping eruption in Florida by Kirby-Smith, Dove and White of which I have had the opportunity of making a very hurried examination in some skin sections submitted to me today (May 25, 1925) by Dr. White are evidently third stage larvae resembling larvae of the superfamily of nematodes known as strongyloides. (The genus Strongyloides does not belong in this group, contrary to what might be inferred from the resemblance of the names. Strongyles, hookworms, trichostrongyles, oesophagostomes, etc., belong in this superfamily). Whether it will be possible from the material available to determine more closely the identity of the worm depends upon the results of further study of the specimens in comparison with the larvae of known species.

SUSCEPTIBILITY

That there should be a difference in individual susceptibility to invasion by the creeping eruption nematode is to be expected. That such a difference does exist has been fully demonstrated through clinical observations. To some patients the itching sensation resulting from infection is almost intolerable, while others endure it with less suffering. The severity of the lesions, too, is more pronounced in some than in others. It is interesting to reflect on the potency of the toxic substance produced by a single larval worm of the species that measures

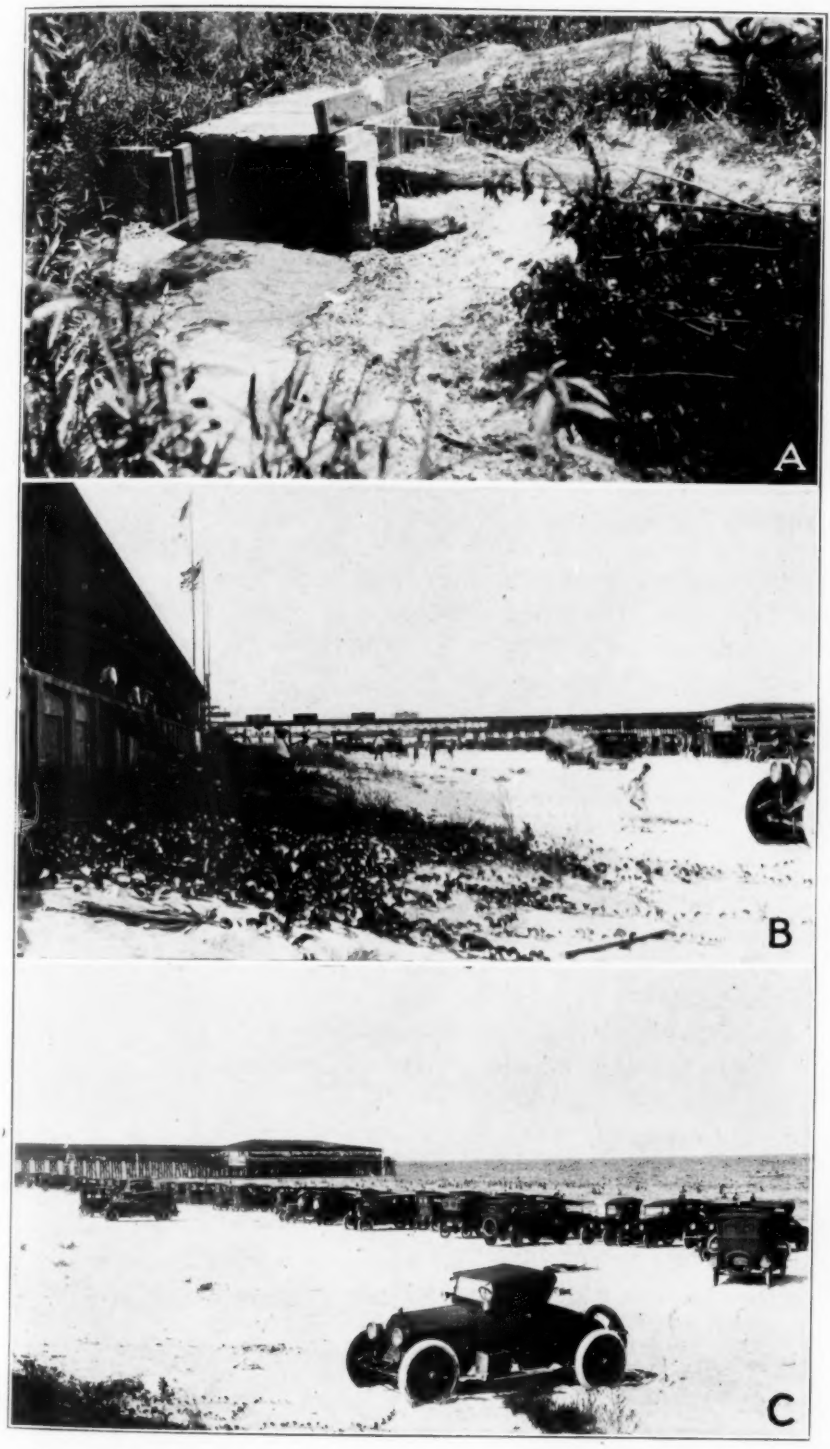

Fig. 7.—Origin of cases of creeping eruption: *A*, drain from swamp containing no sewage; *B*, soft damp sand between high tide and beach buildings, a frequent source of infection; *C*, beach covered by tide, not a source of infection.

only a fiftieth of an inch in length and one twelve hundredth of an inch in breadth.

Some of our observations indicate that some children are more susceptible to infection than others. In one family there were three below school age who lived under identical conditions, and who changed their residence three times within two years. According to the parents, the 4 year old boy, between the ages of the other two, had new lesions of creeping eruption at each place of residence, while the other children had not become infected at any time.

That individual susceptibility is often a natural and not an acquired one seems likely. Some of our patients had lived in the northern states and became infected after going south. That the difference in susceptibility in some instances may possibly be partly due to a sensitization resulting from a previous infection also seems likely. Regarding susceptibility in connection with nematode studies, the work of Ransom [22] and his associates is especially interesting.

Most cases of creeping eruption occur among children. This can be attributed in a measure to more frequent contacts with the soil through being barefooted and through playing. Cases of creeping eruption have been encountered rarely among negroes. In free clinics during 1924, about 300 cases were seen, and of these only three occurred in negroes, one of these being a very black one. Crutchfield [23] reported one case from Galveston, Texas. If members of this race are very susceptible, we feel confident that more of them would have been seen at the city dispensary at Jacksonville, as members of this race are likely to report when they have any ailment. In making a survey as to where white cases originated, negroes and whites were sometimes found living in the same residence block and under similar conditions. In one instance, two white children in the same family and others in different families residing in the same block contracted the malady, but negro children who played with them showed no symptoms.

TRANSMISSION OF THE DISEASE

At least 50 per cent. of the cases of creeping eruption seen by the senior author are believed to have originated at the beach, the probable origin being traced to the soft damp sand in front of the beach buildings at points slightly above the high tide water mark (Fig. 7, *B*). Such patients reported with lesions varying in numbers. They were not the most extensively infected ones. Persons with hundreds of lesions definitely attributed the origin of their infection to contact with damp

22. Ransom, B. H.; Harrison, W. T., and Couch, J. F.: *Ascaris* Sensitization, J. Agr. Res. **18**:577-582 (May) 1924.

23. Crutchfield, E. D.: Larva Migrans, to be published.

sand when they were wet with perspiration while working: repairing an automobile, doing brick work, or making plumbing connections underneath houses, etc. It seems likely that the condition underneath houses is a favorable place for the growth of the parasite and that surface drainage disseminates them, accounting for the observation that light infections are sometimes obtained by children playing nearby at lower levels.

Patients From Whom Larvae Were Recovered.—All of the patients from whom larvae were recovered had multiple lesions, and the histories of these strongly indicates the origin of the infections. Three of the patients had associates who also became infected at the same time and who agreed as to the location where the infection took place.

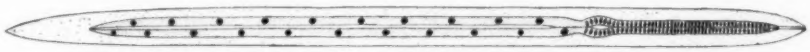

Fig. 8 (Case 165).—Schematic drawing of Agamonematodum migrans reconstructed from microtome sections. The length of the larva in proportion to its width is somewhat greater than that indicated in the drawing.

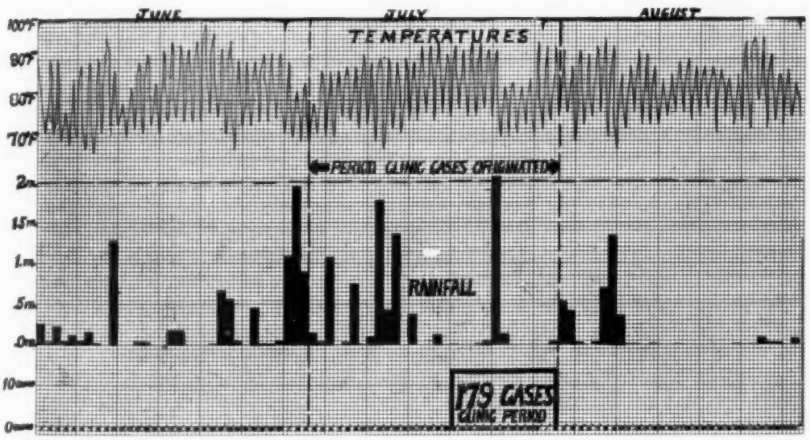

Fig. 9.—Occurrence of cases of creeping eruption as related to temperatures and rainfall in 1924.

REPORT OF CASES

Case 112 (locality, Clermont, Fla.).—An automobile mechanic, aged 45, had at least twenty active lesions on the feet. He had gone fishing with an associate worker in a lake near Clermont, which is about the center of the state and 18 miles from town. There are no homes on the borders of the lake, and at the point visited no evidence was found that any one had been there recently. Both men waded barefooted at the edge of this fresh water lake to catch minnows for fishing bait, and both developed creeping eruption lesions on the feet. As itching was observed by night of that day and neither had come in contact with the soil at any other place than on the edge of this lake, it is believed that this was the source of the infection.

In excisions of skin tissue from the feet, one larva was found in serial sections.

CASE 165 (locality, St. Augustine, Fla.).—A plumber, aged 40, with hundreds of lesions, became infected on the forearm while installing a furnace during the construction of a new school building. His helper was as extensively infected. While both had been on the ground numerous times during the day, it was while making a pipe connection near the base of a small stump that both experienced the same sensation resembling the stinging from nettles. The infection developed similarly and with equal rapidity in both men, the migration taking place on the fifth day. Nine days after the penetration of the larvae, four skin sections were obtained, and from these one parasite was recovered from serial sections. Sixteen days after the infection, four other skin excisions were obtained from the same patient, and one larva was present. What is believed to be a complete series of this parasite in cross section was obtained (Fig. 6).

CASE 199 (locality, Jacksonville, Fla.).—A school boy, aged 11, was infected on the back and forearm at the school grounds while playing football. He did not come in contact with the soil until after school hours. The itching sensation was observed shortly after a fall, and was especially troublesome during that night. Six days after infection, a piece of tissue was removed from the back about the size of a half dollar, from which one larva was recovered in serial sections.

CASE 232 (locality, Waldo, Fla.).—A physician, aged 40, residing on the shore of a fresh water lake, had hundreds of lesions on the buttocks and limbs. He went under his house to superintend repair work, and definitely connected the origin of the infection with this incident. The bricklayer who was doing the work developed a few lesions on one hand. No domestic animals had previously visited this locality, except possibly a cat or a dog. The spot at which the infection took place was in close proximity with sewer pipes, but the joints were tightly sealed, thus apparently preventing soil contamination from this source. Fifty hours after infection one parasite had produced a lesion 1 inch (2.5 cm.) long, while others had apparently been held in check by applications of magnesium sulphate solution and cold packs. Five skin excisions were made from the buttocks, from which one larva was obtained in serial sections. This larva was found in the mucous layer of a hair follicle at quite a depth from the surface of the skin.

Seasonal Incidence and Meteorologic Factors.—Creeping eruption is most prevalent during the summer months, and the greatest number of cases occurs following periods of rainy weather. While a case will sometimes occur during the winter at Jacksonville, infections usually begin about May 1 and continue until about November 1, the greatest number appearing during the vacation period of school children. In the southern part of the state cases often occur in midwinter. Apparently most of them originate in the damp sand areas of the woods where considerable moisture is always present.

Figure 9 covers the school vacation period, the time of the year it would seem the greatest number of persons come into bodily contact with the soil. Between July 4 and August 2, 179 cases originated. It will

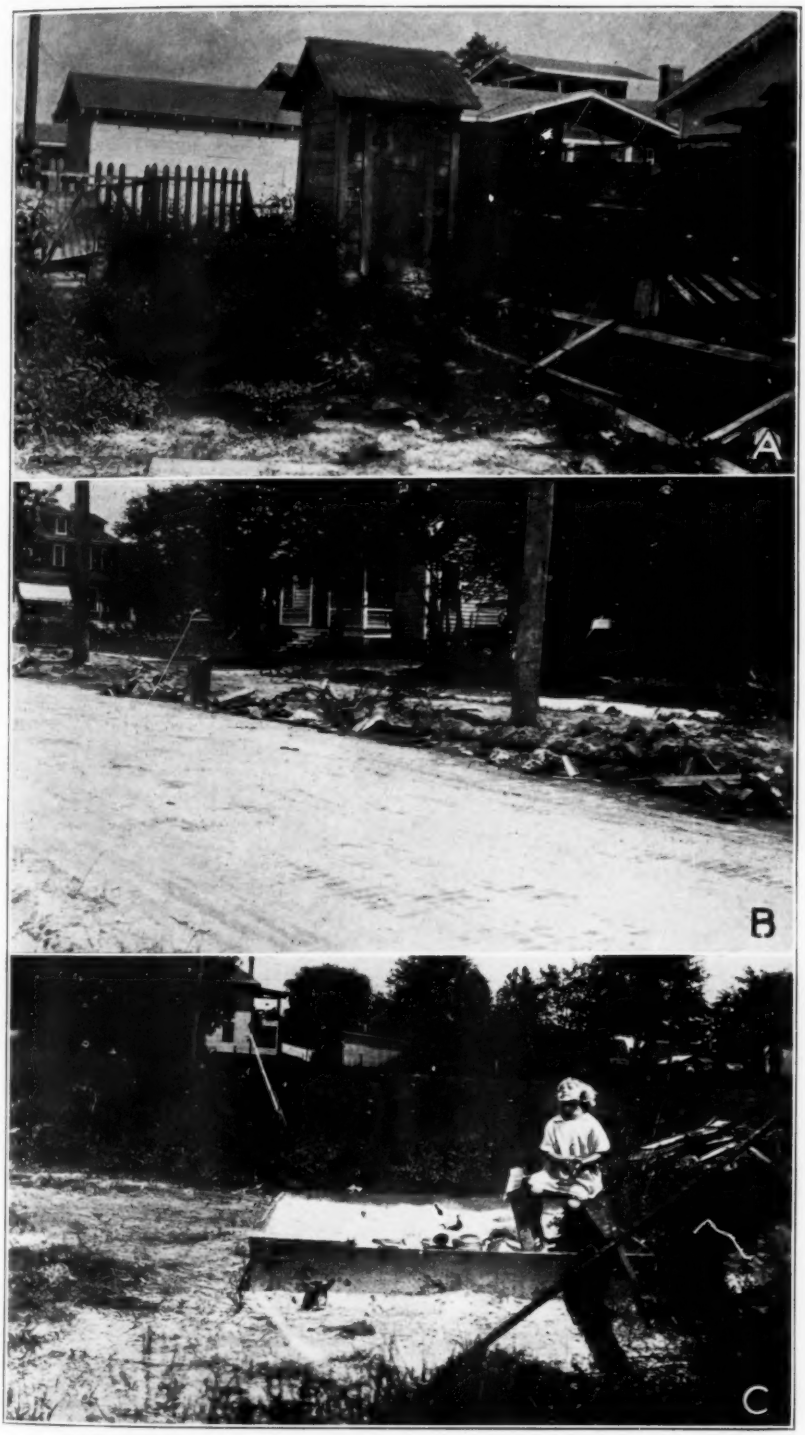

Fig. 10.—Origin of creeping eruption cases distant from the beach: *A*, play place near outdoor privy; *E*, removal of sewage conduit, the origin of numerous infections; *C*, private sand box for children.

be observed that this period was preceded by 4.21 inches of rainfall during June and that on July 1 to 3, inclusive, there was an additional 3.9 inches. A large number of patients traced the origin to the national holiday, July 4, when they were on the beach or picnicking, and when they came into bodily contact with the damp sand.

Following the period shown in Figure 9, there was practically no rain until September 20 to October 10, when there was a total of 13.14 inches of rainfall. Cases again increased with this precipitation, there having been a decline in the intervening period of dry weather. The rains, however, began when the temperatures were slightly lower and when the children were attending school. At this time cases were not as plentiful as during July. From August 2 to November 10 a total of about one hundred cases were reported in Jacksonville. Such a relationship between rainfall and the incidence of cases has been noted during several years by the senior author.

Practically every case originated on sandy soil, which was moist, and which often remained damp on account of the shady conditions. No relationship could be established with the presence of certain trees or plants, but most often the condition was such as to indicate simply that the shade and moisture were important factors. The locations where certain cases originated indicate that the presence of humus or manure, which serve as well as shade in holding moisture at the surface of the soil, were just as favorable for the production of the disease.

ORIGIN OF INFECTIONS

Possible Relationship with Sewage Disposal.—On account of the mild winters in Florida, the smaller sewage conduits leading from the houses are often entrenched at only a slight depth in the soil (Fig. 10, *C*). Sometimes they are partly exposed on the surface, where the sand is damp and where children find interesting places for digging. It would seem possible that through a leakage in the conduit the soil might become contaminated with intestinal worms of man, and that these might be concerned in the causation of this disease.

Case 143 evidently originated near a school building where a conduit was dug up (Fig. 10, *B*) and replaced by a larger one. A number of barefooted school children were infected, and it seemed likely that this was the source of numerous infections.

Some of the cases originated where the soil was probably polluted with human feces. The surface drainage from outdoor privies and the occasional finding of cesspools would indicate that this was a possible explanation.

Most of the cases originating at the beach occurred in children who played immediately in front of the bath houses. Here the sewage dis-

Fig. 11.—Creeping eruption, middle-aged woman, showing multiple uninfected rapidly developing lesions of approximately two weeks' duration, both limbs being involved.

posal pumps were inadequate for prompt removal of the excess water used in shower baths, and there was a drainage toward the surf which could possibly have spread human feces to the play places of children.

Possible Relationship with Intestinal Worm Infection.—The question is frequently asked whether creeping eruption is related to hookworm infections. Most persons who have had experience with those infections recognize the fact that the linear lesion of the former is unlike the "ground itch" of the latter.

For years the senior author has considered the possible relationship between creeping eruption and intestinal worms of man, and on numerous occasions has had examinations made of the stools of patients with creeping eruption. During the summer of 1924 certain patients, who were known to have had creeping eruption previously, were examined by Dr. B. L. Arms of the Florida State Board of Health, and in no case were intestinal parasites found. During March, 1925, specimens of stools were obtained from our most extensively infected patients of 1924, and the findings in them by Dr. Arms were similarly negative. Particular attention was given to the possibility of *Strongyloides* larvae in the latter examinations, for they sometimes occur in man in Florida, but there were no indications of intestinal parasites from any of our patients who had creeping eruption.

In correspondence with Dr. I. L. McGlasson of San Antonio, Texas, we have been informed that he has known of about 100 cases of creeping eruption which originated west of his locality, and that in this section the hookworm does not occur. He has observed that there have been no cases from the eastern section, where the hookworm is known to be common.

Cases Originating Distant from Human Habitation.—The senior author has frequently had patients who attributed the origin of their infection to places at a distance from places commonly frequented by man. Cases 112, 126, 165, 186 and 197 represent such conditions. Some of these were our most extensively infected patients, who had hundreds of lesions. It seems unlikely that the soil was contaminated by human feces in these localities.

Case 165 originated where a new school building was under construction in a wooded area, and at a point on the ground near the center of the building. Two severe cases developed in plumbers from the same spot, being at the base of a small tree stump, where there was no evidence of human excreta.

In a new residence addition, a low area had been filled in by grading and a drainage culvert had been installed for the surplus water. This was not polluted with human feces, but was clear, and furnished an

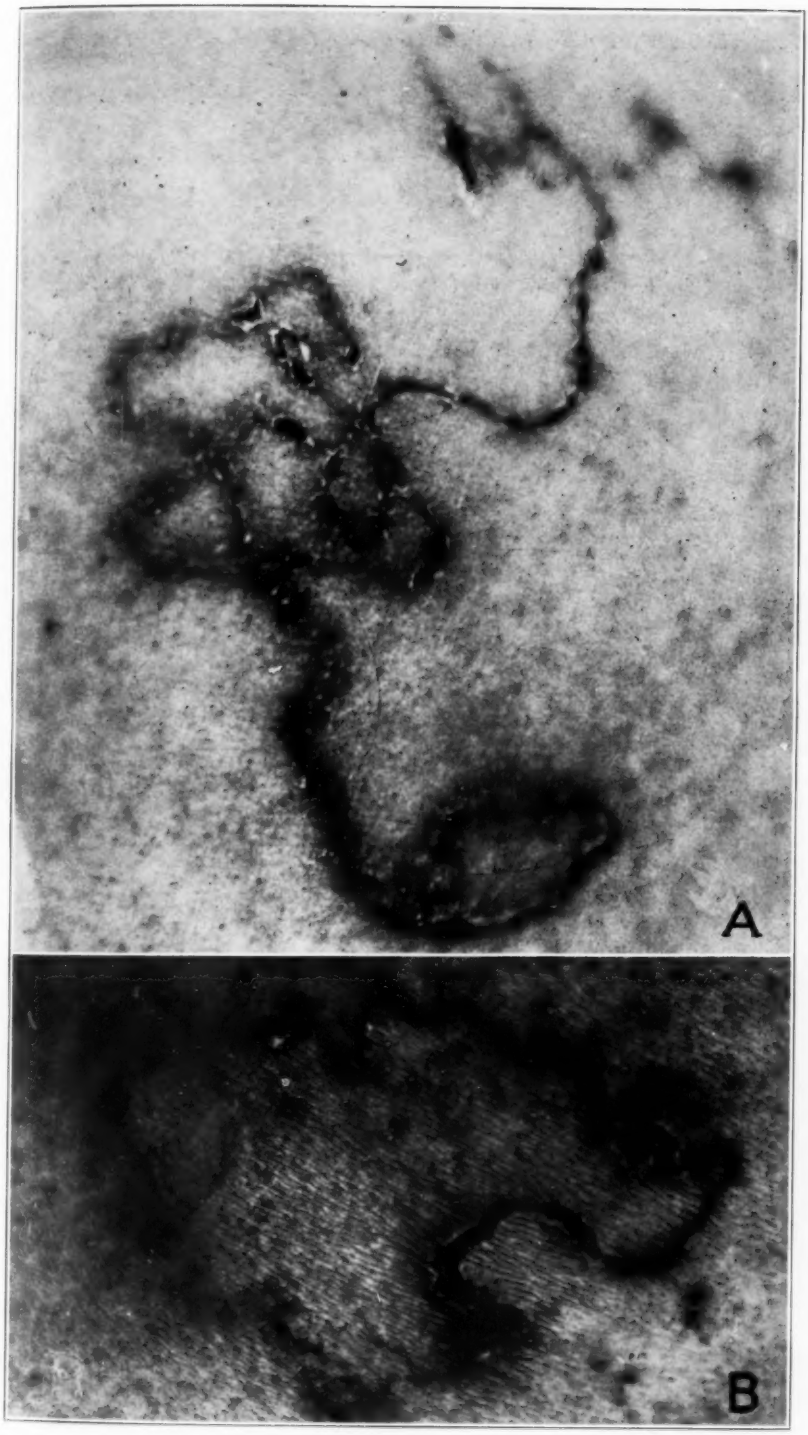

Fig. 12.—Close-up views of lesions of creeping eruption: *A*, unscratched; *B*, ruptured from scratching.

inviting place for barefooted children to wade (Fig. 7, *A*). Those frequenting this stream continued to have lesions on the feet and legs, while other children in the same families who did not wade there did not become infected.

Case 112 originated at the edge of a fresh water lake while the patient was wading barefooted. No one lived on the shores of this lake, and there were no indications that it had recently been visited by other persons. Two became infected here with multiple lesions on the feet.

Cases 186 and 197 had their origin at separate localities, but with similar conditions of automobile trouble on the road. One man (Case 186) crawled under the car in order to make repairs, and became infected with hundreds of larvae across the back. The sandy road was in a low area near a creek bank and had been repaired in places. The other patient (Case 197) was thrown from an automobile when the car went off a new grade to a point where a culvert served the running water. It was necessary to sit on the roadside until help could be obtained. The result was a severe infection across the buttocks and limbs.

According to Dr. I. M. Gunter, the extensive infections seen at West Palm Beach were in persons who had been hunting in the everglades. These did not originate in the muck soil, but in the higher sandy areas which are damp and shady. In these instances, the buttocks were often the portions infected. It is believed that the ingress of the larva occurred while sitting on the sand. These patients are said to have been as extensively infected as those infected from underneath houses.

Dr. Elmo D. French, Miami, Fla., had a patient with hundreds of lesions on the back and shoulders, the infection occurring during the hauling of sandy loam from a graded area. The particular load from which his infection developed had been taken from underneath a concrete sidewalk and transported to the patient's own home. As this was the only occasion he had of coming in contact with the soil, this seems to be a likely source for the infection.

Places Where Infections Originated.—Cases usually have been traced to a bodily contact with damp sandy soil, but in two instances infections were said to have occurred on a porch, the floors of which were old and water saturated at the time of infection.

In one case about fifty lesions appeared on the buttocks of a man after drilling a well. It was necessary for him to sit on the ground while working. The soil surrounding the well came from some depth. This naturally might have been contaminated by an animal.

Children often report that they became infected by wading in water immediately after a rain or by walking through wet grass. Other conditions under which infection is reported are: visiting excavations,

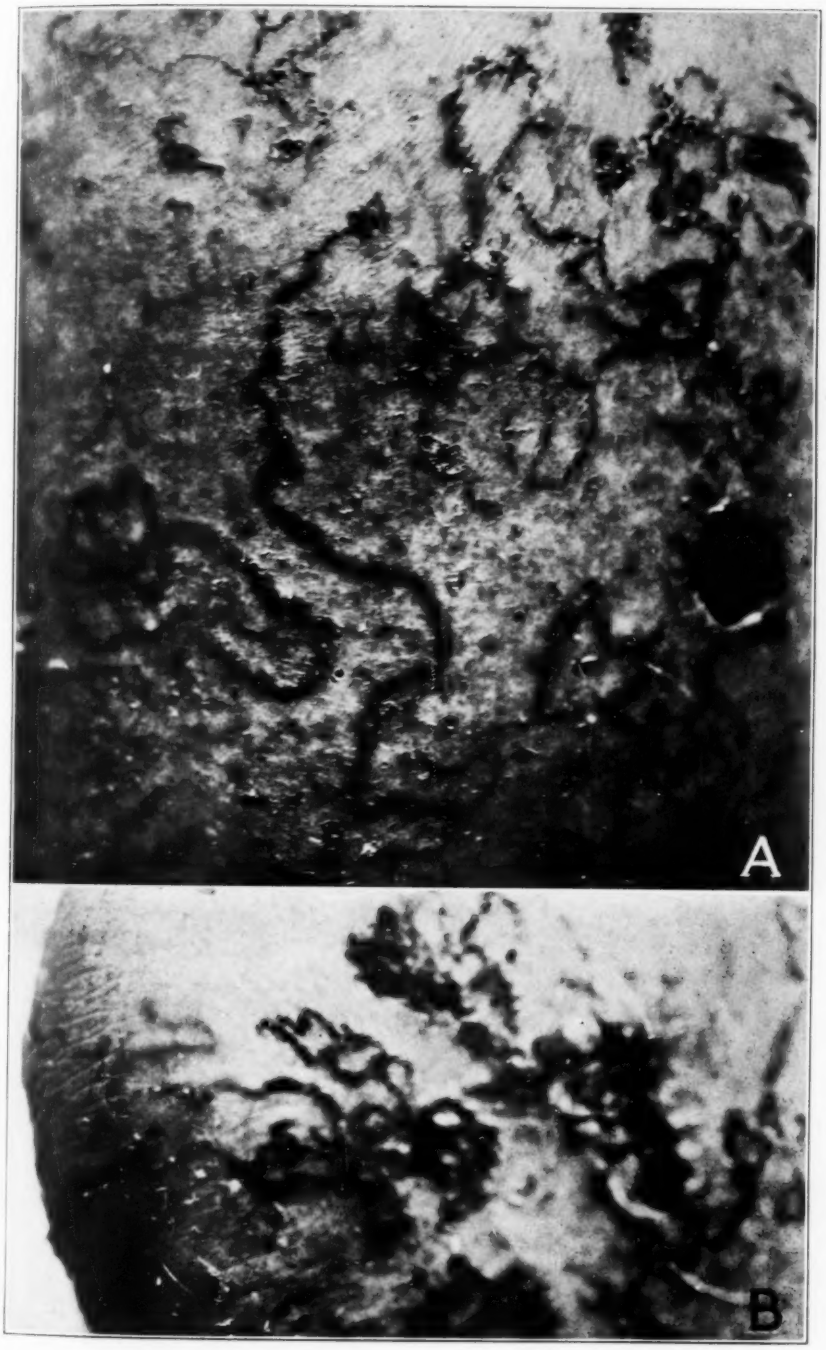

Fig. 13.—Close-up views of multiple lesions on lower limb.

visiting buildings under construction, cutting weeds in an alley, clearing out poultry houses, working in flower gardens, collecting vegetables, falling from a bicycle, playing football, sleeping on the ground in a damp location, digging in the sand near a building or some damp location, and transplanting shrubs. The knees and hands are also said to have been infected from playing marbles on the damp ground. Digging in the sand at points below poultry houses, which would be reached by surface drainage from these houses, has been especially productive of creeping eruption infection.

Possible Hosts and Vectors.—The observations tend to indicate that the nematode causing creeping eruption in man is probably a normal parasite of a warmblooded animal. The occurrence around fresh water suggests that possibly such an animal had been there for water, and that eggs or young stages of the worm had been passed in feces. At the seashore, it is likely that animal life washed ashore might be attractive food for small animals. Certain case histories would seem to indicate that such an animal is of an inquisitive nature and investigates excavations, new buildings and new road grades. It would seem that the host has a preference for culverts under road grades and has the insanitary habit of frequenting sewage disposal places. These facts and the occurrence of cases many miles from human habitation, often in swamps, suggest the possibility that rats may be a normal host or otherwise connected with the transmission of the parasite.

In one suburban section of the city of Jacksonville cases of creeping eruption were more numerous than elsewhere. Here it was learned that during the spring of the year the fields had been burned over so that the young grass was more favorable for cattle grazing. Residents observed an increase in the number of rats about their dwellings, and it seems likely that such a practice in forcing rats into close habitation with man might have had a direct bearing on the occurrence of creeping eruption.

We have not yet been able to correlate the occurrence of creeping eruption with lower forms of animal life. That mosquitoes or ants may sometimes serve as mechanical transmitters of the nematode larva, and that through their bites the nematodes may enter the skin of man is a possibility to be considered. Most of the locations in which cases occurred did not show any evidence of ants, but the sensations experienced by the patients were not unlike that obtained from their bites. No evidence has yet been obtained that the cause of the disease is transmitted mechanically by biting flies, mosquitoes, bed bugs, cockroaches or other insects inside the homes.

Where some cases originated "mole crickets" (commonly known among the boys as "flat heads") were present. We could not correlate

Fig. 14.—Lesions on thigh of adult, duration five or six weeks, migration of parasite retarded by scratching.

the occurrence of these crickets with that of the origin of cases of creeping eruption, but we did find that a number of them were parasitized with nematodes. It is the opinion of Dr. Ransom that these are natural parasites of the mole crickets.

When damp sand was found to contain humus, sometimes mites were observed breeding in it. The presence of mites did not coincide with the occurrence of cases sufficiently to lead one to believe that mites were connected with this skin affection.

Concerning the Ingress of the Parasite.—Our extensive cases have occurred when persons were wet with perspiration and when they were on the damp sand at work. Whether particles of sand make abrasions which serve as points of entry into the skin, and whether the nematode invaders possess chemotropic, histotropic or thermotaxic tendencies which induce penetration are open questions.

In Case 258, the 1 year old baby had played on the sand at home, and had developed a swollen wrist resembling the formation of a boil. The origin of the swelling appeared to be a small scratch, and, according to the mother, this was observed a few days before the swelling started. During the following two weeks countless lesions of creeping eruption developed across the hand and between the fingers. This is the only case in which we can connect the origin to a visible abrasion in the skin.

TREATMENT

Successful treatment of creeping eruption is not easy. While many of these infections respond readily to any one of a number of simple treatments, many others are encountered which prove to be refractory to any known treatment. We do not know that recovery occurs without treatment. There is very good evidence that the parasite is frequently removed by the patient through scratching.

The finding of the causal parasite measurably assists in devising methods of treatment. The usual location of the nematode just beneath the granular layer of the epidermis suggests the nature of a treatment which would give promise of being successful. In such a location the removal of the corneous layer makes the parasite vulnerable to a relatively simple topical application. Such accessibility to the parasite is not always easy of accomplishment. This is especially true when the parasite is beneath the horny layer of the palm, sole, or in the outer sheath of a hair follicle some distance below the surface.

A number of studies have been made on treatment, a summary of which I shall give.

Ethyl Acetate.—This compound has a penetrating quality, and the odor is such that its use is pleasant. In well selected cases splendid results have been obtained. It has been found that it does not injure

Fig. 15.—Multiple lesions on limbs showing impetigenous condition from frequent scratching.

normal skin but has an irritating effect on raw surfaces. In recent cases it has been found more successful than in older ones. In the hands of others similar results have been reported.

When papular lesions are present or when the lesions are only a few days old and have not been ruptured, the free use of ethyl acetate in our experience has been successful. Cotton or gauze should be placed so that the center is well beyond the apparent terminal of the burrow. The acetate is poured on until saturation is accomplished, and then covered with rubber tissue or adhesive tape. One application may accomplish the desired result, but it may be necessary to repeat daily for four or five days. In a case in which there were lesions over most of the back indicating that hundreds of worms had "dug in," more than a half pound of the acetate was used. In this instance all the parasites were killed except two located on the flanks. One further treatment destroyed these. In the use of ethyl acetate the itching is replaced by a cooling sensation, the patient usually sleeping well.

Ethyl Acetate Collodion.—On account of the difficulty of applying ethyl acetate to the skin when the lesions were in close proximity to secondarily infected and raw portions, the idea occurred that a flexible collodion made with ethyl acetate might be efficient. The sulphuric ether was allowed to evaporate, and then an equal amount of ethyl acetate was added.

Eighteen patients were treated by coating an area about and beyond the recent burrows, and "cures" were promptly effected without the use of any other treatment. The period of treatment required varied from two to seven days, with applications twice each day. Such periods probably would have been shorter if the dry collodion had been removed each time before new coatings were applied.

Applications should not be made on old or ruptured portions of the lesions. The acetate collodion appears to work more slowly than the acetate used on gauze or cotton. We believe that once each day the old collodion should be cleaned off so as to remove some of the epidermis. Applications should be made four or five times daily.

Extract of Derris in Ethyl Acetate.—Ethyl acetate was used as a vehicle for testing the effectiveness of other drugs. In recent years powdered derris has come into use as an effective insecticide. It possesses properties of killing certain insects as a stomach poison and certain others by coming in contact with them. Dr. R. C. Roark, of the Bureau of Chemistry, furnished us with a derris extract made with ethyl acetate. It was applied on gauze or cotton after the terminals of the lesions were sponged with the solution. Applications night and morning were effective in five old cases, one of which had resisted

Fig. 16.—Results of previous treatments by patient, duration four weeks.

similar treatments with carbon tetrachlorid. Results with this drug have been of a promising nature. No ill effects on the skin have been apparent.

One Per Cent. Chloropicron in Ethyl Acetate.—A 1 per cent. solution of chloropicron (one of the tear gases used in the world war) in kerosene has been used by Roark and Bishopp in spraying cattle. An approximately 1 per cent. solution of this compound in lubricating oil has been used by them in treating myaisis wounds in goats and other animals. This was done without injury to the animals and was followed by ready healing of the wounds. In view of this, a 1 per cent. solution of chloropicron in ethyl acetate was considered to be sufficiently dilute to permit its testing on human skin. Some successful results were obtained by treating lesions of creeping eruption with this material. The lesion terminals became hypersensitive and painful when the applications were made. The linear lines disappeared during the course of the daily application of such treatments, but the omission of the treatments for two days permitted the larvae to migrate, and the characteristic new lines were observed extending from the previously treated area. The possible dangers of this solution would exclude it for the present from the list of drugs to be used for creeping eruption.

Some Other Methods of Treatment.—If ethyl acetate is not procurable, carbon tetrachlorid can be used in a similar manner but with less success. Some cases have been satisfactorily treated by scraping beyond the visible burrow and applying phenol followed immediately with tincture of iodin. Patients sometimes use tincture of iodin, and sometimes a mercuric chlorid solution. It is the unfortunate combination of these two treatments that not infrequently causes the patients to consult a physician. Due to ill effects and lack of good results, intradermal injections have not proved satisfactory. It is sometimes advisable to clear up a secondary infection with surgical solution of chlorinated soda (Dakin's solution).

Refrigeration applied to the terminal of the visible burrow and the area beyond is probably one of the most satisfactory treatments. The itching sensation of the patient will assist in locating the parasites, and after these points have been marked, they may be frozen with ethyl chlorid spray or carbon dioxid snow. Crushed ice with salt with proper protection for the area surrounding that to be frozen has been used effectively.

SUMMARY AND CONCLUSIONS

Skin infestations in man by larvae of *Gastrophilus, hypoderma* and other flies have been reported from various countries, and it has generally been supposed that creeping eruption was caused by such larvae.

It is now easily seen that different skin diseases have been diagnosed "creeping eruption." Some of these are fly larvae infestations (myiasis).

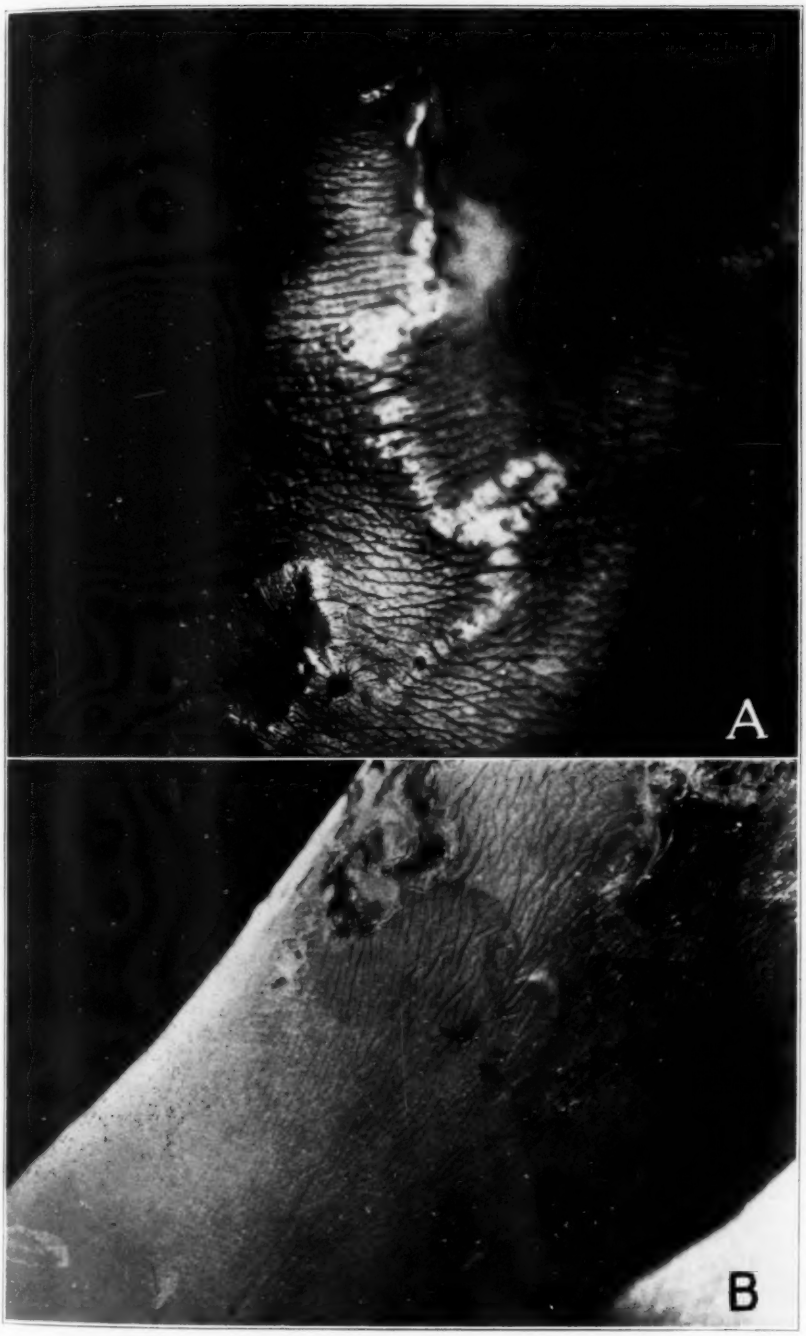

Fig. 17.—*A*, active lesion on forearm showing marked excoriation and infection; duration three weeks; *B*, one well developed lesion on hand of a mulatto boy; duration one week.

others are due to a nematode of the genus *Gnathostoma* (gnathostomiasis), still another disease is caused by a different nematode. For the latter disease the authors have chosen the name "creeping eruption," leaving it to those studying the other creeping diseases to choose suitable names for them. It is this disease that is discussed in the present paper.

It seems likely that the cases reported in the southern and eastern states by Van Harlingen,[5] Stelwagon,[6] Hamburger, Shelmire,[24] Hutchins, Moorhead,[25] Gossman, Haase, Dozier,[26] Edwards,[27] Parham,[28] Gaskill,[29] Whitehouse, Fox,[30] Gray,[31] Klauder and Greenbaum,[32] Ketron,[33] Crutchfield,[23] McGlasson and others,[34] were at least in most instances the disease treated here by us.

The cause of creeping eruption, the disease we are studying, is a nematode larva approximately one fiftieth of an inch in length and one twelve hundredth of an inch in breadth. It was recovered from each of five excisions, representing four patients and as many different localities. More than 200 excisions were made, and of these forty-eight were sectioned serially, making more than 40,000 sections. The causal nematode is reported here for the first time and described under the name *Agamonematodum migrans* by Kirby-Smith, Dove and White.

Some persons are more susceptible to infection than others. Whites are more susceptible than negroes.

Infection occurs more often in children than in adults, and are most frequent during the summer following rainy weather. More cases occur during the vacation period of school children.

Cases in persons most extensively infected have originated underneath buildings when men at work were wet with perspiration and were in contact with the damp sandy soil. Minor infections have often

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occurred in children playing in low areas where apparently surface drainage had disseminated the parasites.

At this time no definite conclusion can be drawn regarding the host of the adult of this nematode parasite.

The origin of some cases in proximity with sewage disposal suggests a possible relationship with intestinal worms of man, while other cases have originated at points distant from such likely sources of contamination.

The evidence at hand tends to indicate that rats might be the normal host of the adult worm. Poultry, cats, dogs and other animals may possibly be concerned.

That insects are concerned in the transmission of the disease is possible.

The inability to locate the parasite definitely has much to do with the difficulty experienced in treatment. When the parasite has invaded the sole or the palm, the difficulty is increased.

Ethyl acetate applied on cotton or gauze or used in a flexible collodion has been effective in many cases.

Refrigeration with ethyl chlorid, carbon dioxid snow, or crushed ice with salt has been used successfully.

DISCUSSION

Dr. G. F. White, Washington, D. C.: I wish to emphasize the fact that more than one disease has been described under the name "creeping eruption." The creeping eruption which Dr. Kirby-Smith has been studying in Florida for fifteen years is different from some of those described in textbooks. Usually insect larvae are thought of as the exciting cause of creeping eruption. Consequently, for the study of its cause entomologists were called on. First, the burrows on the patient were examined, although by this method it was scarcely hoped that the parasite would be found, as Dr. Kirby-Smith had been doing this and had not succeeded. Next excisions were made, and these were dissected, using a binocular microscope, but nothing was found. Serial sections of excisions were then made, and of about fifty of these excisions the five larvae shown on the screen were recovered. The parasite as you have learned is given the name *Agamonematodum migrans* Kirby-Smith, Dove and White. The generic part of this name is used for a certain group of nematodes of which only the larval stage is known. When the adult worm is found, and this will be the next problem, it will be necessary to give another generic name to this causal parasite.

Dr. Everett S. Lain, Oklahoma City, Okla.: It has been my misfortune to have seen a few cases of this disease in Oklahoma—eight during the last fifteen years. I fully agree with Dr. Kirby-Smith as to the distress the patients have and the unrest they given the dermatologist. In the early cases I resorted to various things for relief, having recognized the disease in the first case that was presented. It is easily recognized by the clinical symptoms which were described by Dr. Kirby-Smith. In my desperation I used, or attempted to use, mercury. In the treatment of a desperate case I used about 20 per cent. ammoniated mercury ointment. The patient's friends were not satisfied with

this, and one evening applied iodin. This caused the mercuric iodid vesication and great pain, but it did get rid of the organism. On the next patient we tried this and were fortunate to get the organism, but the treatment is very painful. Then I discovered that Dr. Shelmire had used the ethyl chlorid method of freezing. This is accompanied by a great deal of pain and also the microbe may be overlooked. In a recent case in which I had used the ethyl chlorid and had missed the organism, I thought that as the patient objected so greatly to the vesication, being a child, and as mercurochrome is being used in all conditions, I would try it. I kept it bound to the patient's foot for a week, and the patient has recovered. I give this for what it may be worth, not as a specific treatment. In this particular case it was successful.

Dr. Jeffrey C. Michael, Houston, Texas: Regarding treatment, it is essential to treat the part where the larva is found. It is often difficult to hit the right spot, and it may be necessary for the patient to return several times before success is attained. In my experience, thorough freezing with ethyl chlorid is the most satisfactory treatment when the infestation is limited. I have never seen a case with the tremendous infestation shown on the screen by Dr. Kirby-Smith, and in these cases ethyl chlorid would not be applicable.

Dr. I. L. McGlasson, San Antonio, Texas: People evidently lie on their backs a great deal in Florida. We never see creeping eruption on the back. In our patients it is usually on the legs, because the patients go barefooted. We rarely see it on the hands, and it usually occurs in children. I agree that Dr. Kirby-Smith has done great work along these lines, as witnessed by the rarity with which the larva has been found. The lesion is a traumatic lesion, and the bacillus has gone before the lesion develops, so we usually treat where he is not.

In addition to the treatment mentioned by Dr. Michael, I have used a band of collodion beyond the evident lesion to try to hold the bacillus in that area. You may think this is a small matter, but in children it is no easy problem. Usually, as Dr. Kirby-Smith said, the patients are people who cannot pay you for your trouble. That does not mean that we as dermatologists should not attempt to know all about it. I saw a much more elaborate presentation by Dr. Kirby-Smith on one occasion. I think he has several thousand cases on record and has photographs of all of them.

I am constrained to believe that there may be more than one variety of the parasite. The cases we have seen are rarely of the extensive character Dr. Kirby-Smith has shown. I wonder whether we do not have another variety of parasite that can cause creeping eruption.

I believe that the band of collodion, making use of its contractile effect and the freezing with ethyl chlorid, is the best method of procedure. Dr. Kirby-Smith did not make his treatment very clear to me, and I hope he will tell us a little more about it when he closes the discussion.

Dr. Earl D. Crutchfield, Galveston, Texas: Some cases of larva migrans are seen in Galveston. Some years ago, I began a study of this condition under the impression that probably all cases might not be produced by the same organism. Sometimes patients present only a slightly raised line, while others may present stages varying from a line to large blebs. Some are intensely pruritic, while others are only slightly so. I have seen a mechanic infested with about 200 of these lesions with little or no itching, except at times when the larvae would move away from small tumor masses, where they had apparently become encysted.

Our difficulties in treatment have not been great. I think at least 50 per cent. of the cases will respond to the first application of ethyl chlorid, and the rest will probably respond to one or two more applications. We must remember that we do not know just where the larva is, and we must freeze an area as large as a quarter around the end of the burrow.

We have studied carefully eighteen cases, and by making serial sections we were able to find the larva in two instances, but they were seen only on cross section. I presented this work to a local society, but when I went to a meeting of the Southern Medical Association, I discovered that Dr. Kirby-Smith had 2,500 cases of larva migrans, so I discontinued my work.

Dr. Frederick D. Weidman, Philadelphia: I wish to join the army of those who have testified to the value of Dr. Kirby-Smith's presentation. This disease is not an etiologic entity. Thus, we cannot ignore the reports already made in which the larva of an insect has been dissected out from the burrow, and in which the larva has been allowed to grow on culture mediums, and the adult has been classified. About a year ago a Japanese investigator dissected a *Gnathostoma*—a round worm—from a large piece of skin which he removed. He dissected the worm from the skin at leisure after removal from the patient's body. There is a subsequent report in which *Gnathostoma* was secured from two other Japanese. Evidently there is a variety of parasites which may produce these tortuous sinuses under the skin, and this may explain the different clinical characteristics in the different cases mentioned by the previous discussers. That the disease has been connected up in a rather circumstantial manner with sewage is interesting in connection with the Gordian worm. This is recovered from gutters and is evidently closely related biologically with the one which has been found here in the skin.

PHYSICAL ALLERGY AS A CAUSE OF DERMATOSES *

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A circumstance which possibly justifies my intrusion into dermatologic circles is the fact that the allergic phenomena to be described can be observed more accurately in surface tissues, such as the skin, than they can in the deeper tissues which may be similarly involved. For this reason, an opportunity for accurate study in this line is offered more frequently to dermatologists than to specialists in other lines.

It is well known that patients can become hypersensitive to a large variety of material substances and react whenever they come in contact with them. Some patients are so sensitive that they become ill on contact with minute traces of the agents to which they react. For example, those sensitive to eggs often react to the trace of egg contained in hen meat; those sensitive to buckwheat may be made ill by the trace of buckwheat in a drop of honey; infants sensitive to milk are frequently made ill, not by any of the usual constituents of milk, but by certain foods eaten by the woman or animal furnishing the milk; and finally, patients who receive blood by transfusion are occasionally made ill, or even shocked, by the introduction of one syringe of blood taken from a donor who has eaten some food to which the patient is sensitive.

In this paper, I shall deal, not with illnesses caused by sensitiveness to material substances, but with illnesses of a similar nature caused by sensitiveness to the action of physical agents, such as light, heat, cold and mechanical irritation. Cases of this type have been described in a previous paper under the noncommittal term "physical allergy" (meaning altered reactibility to the action of physical agents).

There seems to be two distinct varieties of physical allergy. They may be related etiologically, but clinically they are very different. In the one type the reaction is confined to the skin area directly exposed to the physical agent (called contact reaction) (Figs. 1, 2 and 3). In the other the reaction may involve not only the skin areas directly exposed, but distant tissues as well, called reflex-like reaction (Figs. 4 and 6).

The contact cases are much the easiest to study. The symptoms in the severer cases which react promptly consist of erythema, pruritus and edema of the skin which invariably appear on suitable exposure of the skin to the agent (light, heat, cold, or mechanical irritation) to

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which the patient reacts. As previously mentioned, the reaction in every case of this type is confined to the area directly exposed, but if a large surface is exposed, constitutional symptoms resembling shock may appear. Depending on the degree of sensitiveness of the patient and the duration and intensity of the exposure, the rash varies in its appearance and in its time of appearance. In patients who are highly sensitive, the symptoms, erythema and itching, often appear within less than one minute. Edema usually appears within a period of six minutes. In patients who are mildly sensitive, a more intense exposure is required to produce reaction, and symptoms may not appear for several hours. In these cases, the hive reaction is not marked, and is followed by anatomic changes in the exposed skin areas, which persist for several days. In fact, in mildly sensitive cases, the reaction following prolonged

Fig. 1.—Urticaria solaris, a type of urticaria factitia caused by exposure of the skin to light. The letters were brought out by exposing the skin through cuts in card-board to summer sunlight for two and one-half minutes.

exposure may not manifest itself as a hive reaction but almost entirely as a dermatitis, characterized by proliferation by the skin epithelium, desquamation and increased secretion.

Opposite to the delayed reaction just described is the so-called solitary reaction (Fig. 5), that is, reaction of a limited skin area which is unusually sensitive. As an example of this may be mentioned a patient sensitive to light who had hives on a certain area of skin near the elbow on exposure of the skin for fifteen seconds to summer sunlight. The hives always had the same shape, size and location and invariably appeared after slight exposure. A more prolonged exposure of the same area of skin would give rise to one large hive which would cover the entire area exposed, completely submerging the so-called solitary reaction.

It seems proper that contact reactions as above described be termed "facticious urticaria" whether the reaction is caused by light, heat, cold or mechanical irritation. Under subheads can be included the type caused by light (urticaria solaris), the type caused by cold (urticaria hiemalis), the type caused by heat (urticaria ab igne), and the type caused by mechanical irritation (urticaria dermographica). In case of delayed reaction, however, when the more intense exposures lead to a dermatitis, the term "dermatitis" should be substituted for the term "urticaria." Since cases of these varieties have been described in detail in previous papers,[1] it seems unnecessary to repeat them here.

Several suggestions were made in previous papers concerning the possible pathogenesis of reactions of this type. Two may be worthy of repetition. In one it was assumed that the patients, coming as they do

Fig. 2.—Urticaria hiemalis, a type of urticaria factitia caused by exposure of the skin to cold. The letters were brought out by rubbing the skin with ice.

from allergic families, may have become specifically hypersensitive to some new body formed in their tissues solely under the influence of one specific physical agent and react to this body just as persons sensitive to pollen react on contact with pollen.

A second possible explanation was as follows: We may presume that in the body we have chemical bodies which are capable of being

1. Duke, W. W.: Urticaria Caused by Light, J. A. M. A. **80**:1835 (June 23) 1923; Urticaria Caused Specifically by the Action of Physical Agents (Light, Cold, Heat, Freezing, Burns, Mechanical Irritation, and Physical and Mental Exertion), ibid. **83**:3 (July 5) 1924; Physical Allergy (Preliminary Report), ibid. **84**:736 (March 7) 1925; Allergy—A Treatise on Hayfever, Asthma, Urticaria, and Allied Manifestations of Allergy, St. Louis, C. V. Mosby Company, 1925.

transformed under the specific influence of certain physical agents to give rise to the nerve impulse which is recognized by the brain as having been caused by that agent. In the terminals of the optic nerve, for example, there must exist bodies which can be transformed under the influence of light to give rise to the impulse in the optic nerve which is recognized by the brain as having been caused by the action of light. Similarly, we must have bodies at other sensory nerve terminals which are transformed by the action of cold or heat or friction to give rise to the respective nerve impulse. These substances under normal conditions must be confined or nearly confined to certain nerve terminals. It is not beyond the realm of fancy to believe that under pathologic conditions, one or more of these chemical bodies escapes from the terminals in which it is normally confined and diffuses through the body, thereby

Fig. 3.—Urticaria dermographica, a type of urticaria factitia caused by mechanical irritation of the skin. The letters were brought out by scratching the skin with a glass slide.

rendering such tissues as absorb it sensitive to a physical agent. For example, if photosensitive bodies in the retina should be distributed by the blood and absorbed in the skin, the skin should become sensitive to light. This would seem analogous to the fact that bile which is ordinarily confined to the biliary and intestinal tract, under pathologic conditions is absorbed, distributed by the blood, and stains the tissues generally, and to the fact that pigment which is normally confined to certain cells escapes from its ordinary areas of confinement under certain conditions, such as melanosarcoma, and lodges in many of the tissues and secretions. It is not unreasonable to suppose that the substances sensitive to light in the retina could under certain circumstances do likewise, and that bodies sensitive to heat and cold and friction could

do the same. It is admitted that this theory to be consistent must depend also on the affected individual being one of allergic strain. Otherwise, the reaction should be inflammatory in nature rather than edematous.

Whereas the contact reactions just described are interesting and important, the reflex-like reactions are the more common and give rise to a more varied clinical picture. As previously mentioned, "reflex-like reaction" is a term used in describing reactions which are not confined to the surfaces directly exposed to the irritating agent, but which involve distant structures as well (Figs. 4 and 6). Frequently they involve distant structures only. In this case, the relationship between cause and effect may be difficult to discover. Reflex-like reactions, so far as the skin is concerned, have all been caused, in my experience, by the effect of heat or cold.

Fig. 4.—Urticaria calorica, a reflex-like reaction caused by exposure of the right shoulder to the heat of a nitrogen lamp for fifteen seconds.

Frequently patients sensitive to heat react only after previous exposure to cold and vice versa, and patients sensitive to cold react to cold only after previous exposure to heat. These two types are not separated from the others because of the fact that in every case a change in the temperature, rather than a constant temperature of any given grade, seems to be the controlling factor.

As with constant reactions, so with reflex-like reactions, there are three different types of reaction, namely: the immediate reactions, consisting of erythema, pruritus and edema, that is, urticaria; delayed reactions in which the urticarial reaction is slight and is followed by dermatitis; and, finally, solitary reactions (Fig. 6) which consist of wheals or other skin anomalies covering limited areas and appearing under the influence of extremely small amounts of heat or cold as the case may be.

Sensitiveness to heat is more common than sensitiveness to cold. Reactions are characterized in highly sensitive cases by a generalized rash (erythema, pruritus and, less often, urticaria) which appears under the influence of heat however applied, whether through the use of a hot compress, a hot lamp, a diathermic or autocondensation current, by the drinking of hot water or even under the influence of heat generated by physical or mental exertion. In highly sensitive cases the rash can be brought out by having the patient place his hand for a moment in warm water or even by the heat generated by such exercise as putting on an overcoat, walking up a few steps or even by turning over in bed quickly. Heat generated by an argument, by the excitement of watching an athletic contest or even by an interesting business deal is often sufficient to cause the rash. The rash can be stopped immediately or prevented by the application of cold, such as by the removal of clothing,

Fig. 5.—Urticaria solaris, a solitary reaction caused by exposure of the skin to sunlight for a few seconds. A more prolonged exposure gave rise to a hive which covered the entire area exposed.

by having the patient place his hand in cold water or by drinking cold water. It was estimated in one highly sensitive case that the generation of one calory of heat by exercise was sufficient to bring out the rash if the patient was warmly clad.

The rash is characterized in highly sensitive cases by erythema, itching and hives, which usually appear within one or two minutes and last from five minutes to half an hour. In less sensitive cases the time of appearance of the rash may be delayed and in this case lasts longer and may appear as angioneurotic edema rather than as superficial urticaria. In patients who are less highly sensitive, the rash may be characterized by general redness of the skin, proliferation of the epithelium and desquamation. In the case of solitary reactions, the manifestation may

be wheals or papules which appear under the influence of remarkably little heat. In one case, for example, several wheals would appear on the chest (Fig. 6) under the influence of the slightest excitement or exercise or after exposure to the smallest amount of heat. Rashes which are apparently caused by excitement or emotional disturbance often belong in this category.

Reactions caused by cold are similar to those caused by heat, except that they are relieved by heat or physical or mental exertion. In several cases of asthma due to sensitiveness to cold, the symptom asthma could actually be relieved by physical or mental exertion. In one case a marked attack was actually relieved by a fistic encounter. One could surely count on the fact that this would have made symptoms worse rather than better if they had been caused by anything other than sensitiveness to cold.

In a majority of cases reaction caused by heat or cold follows change in temperature rather than exposure to a temperature of any

Fig. 6.—Urticaria calorica, a solitary reaction on the chest brought out by heat and exercise.

specific grade, that is, patients sensitive to cold react more markedly as a rule if they are previously exposed to heat, and those sensitive to heat react more markedly if previously exposed to cold. For this reason, those sensitive to heat frequently have their symptoms in most marked degree during the winter months and vice versa, persons sensitive to cold react most markedly during the summer months. This frequently gives rise to misleading histories, for the patient as a rule attributes his illness to the very element which actually relieves him. For example, one patient vowed that his reaction, urticaria, was caused by cold. On testing, however, it was found that reaction could not be produced by cold but could be produced by heat, especially if he were previously exposed to cold. He stated with great positiveness that his rash was caused by exposure to cold winds and cold water—in fact, to

cold of any source. On careful observation, however, he found that symptoms would never appear during his exposure to cold but a short time after he began to get warm. Cases of this variety occasionally gain tolerance through frequent exposure, and for this reason give seasonal histories, that is, a history of attacks occurring during the first warm days of spring or summer or during the first cold days of fall or winter. Since reactions of this type have been described in detail in previous communications, it is needless to repeat them here.

The diagnosis of reflex-like reaction is not difficult, and can be proved objectively in persons who are highly sensitive and react promptly. In case of delayed reaction, however, the diagnosis is extremely difficult and uncertain and can often be made only by comparing the behavior of symptoms with those of patients who react promptly. Heat sensitive patients often run a subnormal temperature and react on a rise in temperature. In cases of this type, the degree of sensitiveness is greatest when body temperature is lowest and often disappears when body temperature remains about normal. In one patient subject to chronic urticaria and angioneurotic edema, symptoms disappeared invariably when she left home. On her third visit to me in Kansas City, it was learned that her home environment was depressing, and that she was subject to fits of temper when displeased by her husband; a rash would usually appear one or two hours afterward. It was found that while at home her temperature was markedly subnormal and that with displays of temper, her temperature would rise and that the rash would follow. When she moved to an environment which pleased her, her body temperature would remain relatively normal. It was possible in this case through simple change in environment to rid her completely of her illness.

A theoretical explanation for reflex-like reactions caused by heat or cold is difficult. One might call the phenomena a simple reflex. This would amount to nothing more than placing a cloak of knowledge around uncertainty. An adequate explanation needs be more detailed than this.

The mechanism involved in reflex-like reactions would seem to be more complex than that involved in contact reactions. In contact reactions the tissues chiefly affected are those which are directly exposed to the irritating agent. With reflex-like reactions, however, the tissues involved may be distributed over a very large part of the entire body.

One might advance the same theories in this connection which were used in an endeavor to account for contact reactions. We might assume that the action of the physical agents in the contact cases was direct on peripheral tissues or peripheral efferent nerve endings, while in the reflex-like cases the action was exerted on sensory or afferent nerve terminals. Through the latter abnormal impulses might be generated

and transmitted to the autonomic nerve mechanism, and there give rise to explosive impulses which might manifest themselves as reactions.

The underlying condition responsible for the reflex-like reactions seems to me to be one of an injured nerve mechanism. One might go further and say that it seems to be a pathologic reaction of the heat regulating mechanism. It seems remarkable that warm-blooded animals are able to maintain a constant body temperature under such varying conditions of heat and cold, moisture and dryness of the air, rest and functional activity, as the majority are subjected to. Body temperature under normal conditions is maintained at a constant level through complicated reactions which vary the caliber of the surface vessels and vary the secretion of moisture from the skin, nasal and bronchial mucous membranes. When the heat regulating mechanism is normal, body tem-

TABLE 1.—*Types of Cutaneous Reaction Caused Specially by the Action of Physical Agents*

CONTACT REACTIONS
Immediate Reactions (Urticaria Factitia)
Urticaria solaris (caused by light)
Urticaria hiemalis (caused by cold)
Urticaria dermographica (caused by friction)
Urticaria ab igne (caused by heat)
Delayed Reactions
Dermatis
Solitary Reactions
Wheals and papules
REFLEX-LIKE REACTIONS
Immediate Reactions
Urticaria calorica (caused by heat)
Urticaria frigore (caused by cold)
Delayed Reactions
Dermatis
Solitary Reactions
Wheals and papules

perature can be maintained at a remarkably constant level under the most varied external and internal conditions. It seems within the realm of good reason that this mechanism at times may be injured, and when injured may react in an abnormal manner, not only in relation to the dilation or contraction of vessels, but also in relation to secretion and activity of nonstriated muscle in general. If such an abnormal mechanism should exist in a person of allergic strain, it seems conceivable that this mechanism might give rise to the peculiar manifestations of allergy which we ordinarily term asthma, allergic coryza, urticaria, angioneurotic edema, etc.

One might advance in support of such a theory the fact that a very large proportion of patients who are subject to reflex-like reaction caused by sensitiveness to temperature change date the onset of their symptoms from a severe illness—often an infectious disease.

SUMMARY

Physical allergy is a name suggested for altered reaction caused specifically by the action of physical agents such as light, heat, cold and mechanical irritation, and in the case of heat sensitiveness, indirectly by the effect of mental or physical exertion.

The reactions produced are of two varieties: (1) contact reactions in which the reaction is confined to the point of contact between a surface and the irritating agent; (2) reflex-like reactions which occur not only at the site of contact but in distant structures as well. General symptoms follow contact reactions if the surface exposed is large enough.

The cutaneous symptoms vary with the degree of sensitiveness of the patient and with the intensity of the exposure. In highly sensitive cases in which reaction appears promptly, the most constant symptoms are erythema and pruritus and in the more marked cases, superficial urticaria. In the case of delayed reaction, angioneurotic edema is frequently observed. In many cases of delayed reaction, the hive reaction is not marked and is followed by dermatitis characterized by proliferation of the tissues, desquamation and increased secretion. Solitary reactions may occur after remarkably slight exposure and appear in the form of wheals or papules over limited areas.

DISCUSSION

DR. EVERETT S. LAIN, Oklahoma City, Okla.: Dr. Duke spoke of one of the severe cases from Oklahoma. I do not know whether we are more thick blooded or more thin blooded, or more prone to fight with our wives, but I see a number of cases. At present, it is my misfortune to have two persistent ones, persistent in that the patients are persistent in seeking relief and in asking me to try something else, and I have already exhausted the pharmacopea. Although it may not be within the province of Dr. Duke's paper, since he discussed so many etiologic factors, the important thing to me is whether or not he has been able to relieve any of his patients.

DR. CHARLES M. WILLIAMS, New York: I recall seeing a man in Paris who developed a severe urticaria on exposure to cold, especially after a cold shower or spray. The effect was immediate, and probably due, therefore, to a nervous reflex, perhaps psychic. It may be that all these curious, sudden urticarias are psychodermatoses. I would like to ask whether Dr. Duke has ever tested his patients by putting them under the influence of chloroform or ether, and then applying heat or cold. If the phenomenon is due to a local chemical change, it should not be altered by narcosis.

DR. J. FRANK SCHAMBERG, Philadelphia: I am sure we are all indebted to Dr. Duke for bringing this interesting and important subject before us. We know his extensive work along the line of allergic investigation. We know that the wheal is the most common cutaneous expression of allergic phenomena, and yet the wheal may express something besides that. We are all familiar with the cases of severe and persistent urticaria which have occurred after psychic shock. I know a man who was head of a research laboratory and thought he was responsible for an explosion which occurred. He imme-

diately developed an urticaria which persisted for many months, with some loss of control of the blood vessels. Then, too, we know that the physical things acting in this way may produce conditions about which we know little. We have found that the exposure of the skin of rabbits to the ultraviolet light has much influence in increasing the lipolytic power of the blood and skin. The light increases the lipolytic power of the blood and skin.

Dr. F. J. Eichenlaub, Washington, D. C.: In connection with Dr. Duke's paper, the following case is of interest. A young man who had had a streptococcic tonsillitis on several occasions in the past, consulted me for an eruption on the backs of the hands and arms, and on the face and neck, which recurred every spring on those areas which were first sunburned. The eruption was a typical erythema multiforme, and was sharply limited to the areas of a recent sunburn. The tonsils were removed, and for the past two springs the eruption has not recurred. The physical agent in this case precipitated the attacks. I think we should be careful to remove all such possible factors before assuming that purely physical agents can produce such effects.

Dr. W. W. Duke, Kansas City, Mo.: I realize that I could hardly make clear so complicated a subject as physical allergy in the short time at my disposal. Furthermore, I do not believe it possible to convince any one of the reality of this condition unless he has had personal experience with it. The best patients for study are those who are excessively sensitive and react promptly. In one case an urticarial rash was actually brought out by as little as one calory of heat regardless of how it was applied, whether through the heat of a nitrogen lamp, a diathermic current, the drinking of hot water, or by physical or mental exertion. The rash could be prevented or stopped immediately by cold regardless of its source, whether through the drinking of a little cold water, by fanning, or by the removal of clothing. Illness brought on by heat, mental or physical exertion, should always suggest the possibility of heat sensitiveness. Urticaria, erythema, or pruritus brought on by laughing, crying, or emotional disturbance should always suggest the possibility of heat sensitiveness. Chloroform or other anesthetics tend to relieve asthma. The same may be true of the reflex-like reactions which cause urticaria. The heat method of treatment is the avoidance of the cause. Avoidance of the cause is not always possible, however. In this case treatment with the agent which causes reaction with a view to increasing tolerance should be tried. This occasionally is beneficial in the milder cases. It works best apparently in urticaria dermographica, which can often be completely relieved subjectively by scratching the skin, generally at frequent intervals with a very stiff brush. Occasionally persons sensitive to heat can be given tolerance to heat through frequent hot baths. Thyroid extract given with a view to raising body temperature was useful in two instances of sensitiveness to heat. Insulin was useful in one case and nonspecific vaccine therapy given for the purpose of elevating temperature helped several. Any agent which improves general health is likely to reduce the severity of the symptoms, especially those sensitive to heat who on relief of any debilitating influence either mental or physical, are likely to become more tolerant of heat.

CUTANEOUS REACTION IN LEISHMANIASIS

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The clinical diagnosis of cutaneous leishmaniasis in the majority of cases presents no difficulty. This is not true, however, of the lesions of mucous membranes, particularly in those cases in which there are no associated lesions of the skin. In such cases the differential diagnosis from syphilis, tuberculosis and blastomycosis may not be easy. Search for parasites in smears and sections is frequently negative, particularly if specific therapy, such as intravenous injections of tartar emetic, has already been instituted. The histologic features of the lesion, though easily distinguished from tuberculosis and blastomycosis, may be confused with syphilis. The therapeutic test, that is, the administration of tartar emetic, may give no aid, since, as is well known, the mucous lesions are notably refractory to treatment. Antisyphilitic treatment might be more helpful, though there would remain the possibility of a third undetermined infection in those cases in which the Wassermann reaction was negative, antisyphilitic treatment ineffective, and in which the search for *Leishmania* is also negative. In such cases the cutaneous reaction, as will be shown in the following report, is a valuable aid in diagnosis.

A few months ago, Mrs. Wagener,[1] studying guinea-pigs immunized with strains of *Leishmania tropica* (oriental sore) and *Leishmania infantum* or infantile kala-azar, succeeded in obtaining through the use of an alkaline extract of these strains a cutaneous reaction, characteristic and specific. The results of these investigations stimulated us to study the reaction in cases of human leishmaniasis, using an extract prepared from strains of organisms obtained locally.

PREPARATION OF EXTRACT

A profuse growth of *Leishmania* is obtained on Nicolle's[2] medium after from fifteen to twenty days. The culture is removed from the medium with physiologic sodium chlorid. The suspension is centrifugalized, and the sediment is washed and centrifugalized, and the process is again repeated. To the sediment from the last washing, Coca's[3]

1. Wagener, Edna H.: A Skin Reaction to Extracts of Leishmania tropica and Leishmania infantum, University of California Publication in Zoology **20**:477, 1923.

2. Nicolle, C., and Comte, C.: Sur un trypanosome de chauve-souris, Arch. de l'Inst. Pasteur de Tunis, April, 1908, No. 2, pp. 69-74.

3. Coca, A. F.: J. Immunol. **7**:163-178, 1922.

fluid is added in sufficient quantity to make a definitely turbid suspension. The liquid is then covered with toluol and left at room temperature for three days. The container is shaken daily to facilitate maceration. At the end of this time the suspension is again centrifugalized, and the clear liquid above the sediment is pipetted off. This is the extract. Before using, its sterility must be tested by cultures in simple gelatin, incubated at 37 C. and in Nicolle's medium at room temperature.

In the preparation of our extracts, only two strains of *Leishmania* have been used, one isolated by me from a patient who had contracted the disease in Araçatuba, a small town in the state of São Paulo, and the other kindly sent me by Mrs. Wagener through Dr. Noguchi. The extracts of these two strains were, of course, prepared separately. Mrs. Wagener in preparing the extracts washes the organisms from the surface of the culture mediums, centrifuges the suspension, extracts the hemoglobinic liquid and adds Coca's solution. We prefer, however, to wash the cultures three times in order to eliminate all the hemoglobin. With the extract prepared in this way we have obtained specific reactions, but it has seemed to us that toluol added during the preparation of the extract causes them to produce a cutaneous reaction. Therefore in the extracts which we have more recently prepared, toluol, which is apparently unnecessary for preservation, has not been added.

The second extract used consisted of two portions, one made from the Brazilian leishmania and the other from *Leishmania tropica*, or oriental sore. We followed the technic already described in making the first portion, omitting, however, toluol. With both portions we succeeded in obtaining a weak though specific reaction. It seemed that the weakness of the reaction was due to the insufficient numbers of the micro-organisms employed.

The third extract made from Brazilian *Leishmania* was prepared in the same way as the second except that a larger supply of *Leishmania* were used. In the preparation of this extract we preserved the hemoglobinic liquid from the first washing, adding to it 4 per cent. phenol, and tested the liquid by intradermic injection in order to determine its potency. This extract proved quite as good as the first, and the hemoglobinic liquid of the first washing was found capable of provoking sharp and specific reactions although the reactions were weaker than those produced by the extract proper. This suggested to us the idea of preparing an extract which would include the metabolic products of *Leishmania*. To this end we placed a culture of *Leishmania* in Nicolle's medium for the period of one month and added to the culture equal parts of Coca's fluid. After three days' incubation, the extract was tested, but failed to give satisfactory results.

METHOD OF INJECTION

The injection must be made intradermally. This is easily accomplished with the short, fine needle. The injection results in the formation of a pale, rounded papule in which are seen punctiform depressions due to the presence of hair follicles. The quantity of extract usually injected is about 0.2 c.c., but we preferred to be guided in the discharge by the dimension of the papule. When the papule reaches a diameter of about 8 mm. the needle is withdrawn.

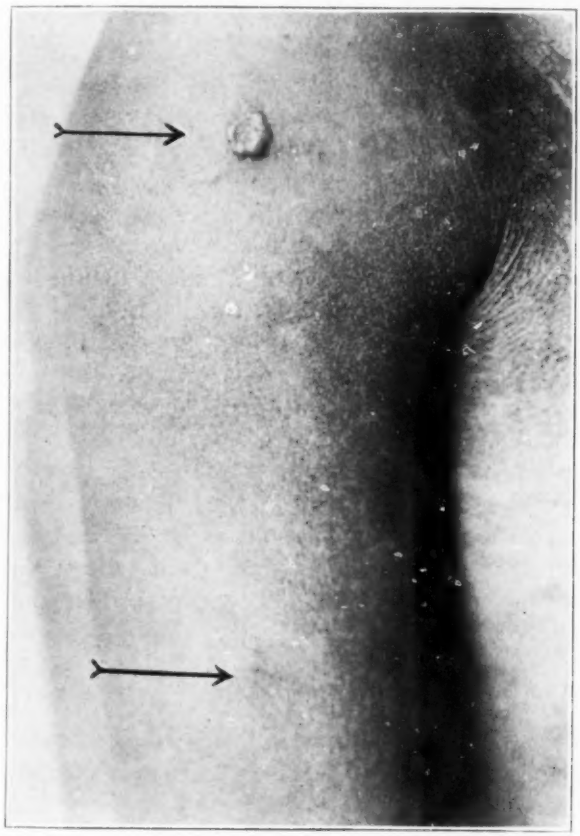

Fig. 1.—Vesicle formation skin reaction to Leishmania extract.

CHARACTER OF THE REACTION

In the positive cases, at the end of twenty-four hours there is noted a rounded area with a diameter two or three times that of the original papule produced by the injection. The area is red, congested, and has a consistency greater than that of the surrounding skin, and is easily palpable. In some cases the center of the papule remains pale and clearly defined; at other times, all one sees is a punctiform hemorrhage in the

center, due to trauma caused by the needle. The intensity of the reaction naturally varies in different cases. In some persons some vesicles are formed which become transformed into transparent pustules. Such lesions are later covered by crusts. The reaction lasts several days and disappears slowly. It is generally most intense at the end of the first twenty-four hours. We have never observed late reactions. Heat, pain and itching are sometimes noted. None of our patients has ever complained of fever, chills, or other systemic reactions. Immunologically the reaction is comparable to that of tuberculin. It is clearly of the nature of sensitization of the skin (allergy) in localization.

INJECTIONS

Injections should be made preferably in the deltoid region after it has previously been washed with alcohol. The alkaline extract is injected on one side and an equal quantity of Coca's fluid on the other as a control. As a matter of experiment we made some injections in the anterior surface of the forearms in order that the patients might observe the evolution of the reaction, but in this region the reactions were less pronounced. A poorly defined, erythematous area was seen, from which extended radial striations. The striations extended along the veins. Since in negroes it is not possible to observe an erythema of the skin or the arm, we made the injection in the thenar portion of the palms. The results were not satisfactory on account of the thickness of the epidermis, which in our patients, all of whom were laborers, was pronounced. It was noted that the positive reactions in these regions were painful. An attempt to produce a conjunctival reaction by the installation of two drops of extract in the conjunctival sac was negative. Owing to the alteration in the consistency of the skin by reason of the congestion and perhaps infiltration, we found it possible to observe cutaneous reaction even in negroes.

CLASSES OF PATIENTS

The patients used in these experiments were cared for in the wards of the dermatologic service of Professor Adolpho Lindenberg. In addition to those with leishmaniasis we injected also as controls a number of persons suffering from other diseases. Some of the patients with *Leishmania* had received local treatment, others had had intravenous injections of tartar emetic or intramuscular injections of bismuth salts. There were all stages of healing. A majority of the patients showed lesions of the mucous membranes. All the patients were males at ages varying from 7 to 70 years.

The diagnosis was made on the basis of clinical observation. We did not attempt to confirm the diagnosis by the demonstration of specific

micro-organisms, because almost all the patients had been subjected to treatment, which, as is well known, causes either the rapid disappearance of *Leishmania* or makes them scarce and difficult to demonstrate.

RESULTS OBTAINED

After preliminary experiments which established the potency of the extracts, our investigations were begun. We made injections into thirty-seven patients who had lesions, and obtained positive reactions in thirty-two. Of the five patients who gave negative reactions, one was

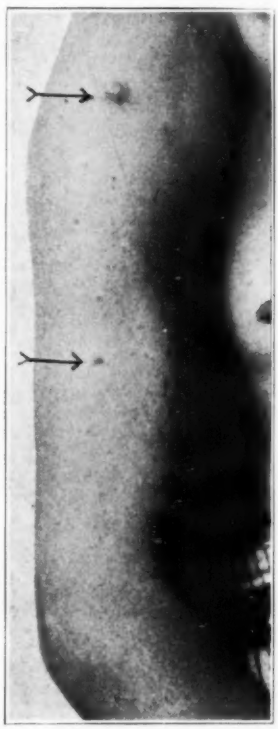

Fig. 2.—Erythematous reaction to Leishmania extract.

a boy of 14, a congenital idiot with almost healed lesions; another was a robust man of about 35 years, with a single ulcer of the foot in which healing was advanced; a third was a husky Portuguese with extensive verrucous *Leishmania* of the margin of the nose involving both skin and mucosa; the fourth had pemphigus foliaceus and leishmaniotic ulcers; and finally, another well nourished white man with extensive lesions of the pharynx and the palate in addition to two typical cutaneous lesions. The Portuguese man just referred to had been sick for more than two years. The Wassermann reaction as well as the examinations

of smears and sections of the lesions for *Leishmania* were negative; this patient was treated with injections made of *Leishmania* killed by a temperature of 50 C., the injection being given intramuscularly every four days until six had been given. No improvement was noted. Eight days after the last injection we repeated the cutaneous test with the same negative result. This observation suggests that the individual was probably not capable of reacting against *Leishmania*, and would thus explain the original negative reaction. It should be explained in this relation that Mrs. Wagener has shown that rabbits immunized with a suspension of *Leishmania* in physiologic sodium chlorid gave a cutaneous reaction. While we have not yet established the fact that this is true also of man, we would expect in the light of

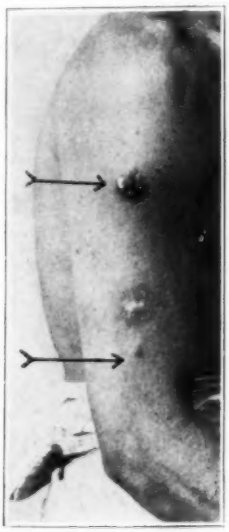

Fig. 3.—Pustule formation to Leishmania extract.

the experimental studies that such would be the case. I am convinced, too, on the basis of our investigation, that a majority of cases of leishmaniasis give a positive reaction. The percentage of negative findings, 13.5 per cent., in this series is not greater than has been observed in syphilitic reactions to luetin. Of thirty-six cases used as control, in which there was no evidence of leishmaniasis, we obtained negative reactions in thirty-three and doubtful reactions in three. Of those with doubtful reactions, one had syphilis, another had an ulcer of the foot, and the third, scabies.

DOUBTFUL REACTION

Neisser, in studying the cutaneous reaction in syphilis, called attention to the susceptibility of the skin of such patients to trauma. To

this phenomena he gave the name, "Umstimmung." In the beginning we thought that the doubtful reactions perhaps were of this nature. As a matter of fact, the same type of doubtful reaction was observed occasionally following the injection of Coca's fluid, particularly in cases of leishmaniasis which had given a clear positive reaction with the extract. In these cases, however, the intensity of the reaction following the extract was very much more marked than that produced by Coca's fluid.

Among the controls, i. e., cases free from *Leishmania*, there were five with striking positive Wassermann reactions, but with absolute negative reactions to the *Leishmania* extract. This observation indicates that syphilis does not tend to produce positive reactions to the *Leishmania* extract. It is my opinion that these doubtful reactions are simply the result of the sensitization of the skin of the particular individual.

Cutaneous Reaction in Various Conditions

Disease	Number of Persons Tested	Reaction		
		Positive	Negative	Doubtful
Leishmaniasis	37	32	5	—
Syphilis	11	—	10	1
Eczema	4	—	4	—
Lupus erythematosus	1	—	1	—
Chronic osteomyeletis	1	—	1	—
Erythema solar (sunburn)	1	—	1	—
Indolent ulcer of the foot	2	—	1	1
Pemphigus foliaceus	1	—	1	—
Pyodermitis	1	—	1	—
Scabies	2	—	1	1
Pruritus	1	—	1	—
Cases free from symptoms of leishmaniasis but undiagnosed	11	—	11	—

SUMMARY AND CONCLUSIONS

1. Intradermal injections of an alkaline extract of *Leishmania* were given to thirty-seven patients with leishmaniasis, and positive reactions were obtained in thirty-two of them, or 86.5 per cent.

2. Injections with the same extract were also given to thirty-six persons free from leishmaniasis. Of these, thirty-three developed negative reactions, and three showed a certain reaction definitely distinct from the specific reactions obtained with the patients who had leishmaniasis. It was much less intense.

3. The cutaneous reaction of leishmaniasis is specific, and for this reason when typically positive is of itself sufficient to confirm the diagnosis, if the patient has never had leishmaniasis before.

4. A negative reaction reduces to 13.5 per cent. the possibility that the disease is leishmaniasis.

5. The result of the reaction should not be accepted without knowledge beforehand concerning the specific value of the extract.

6. Positive reactions were obtained in all stages of healing.

7. The extract prepared from a strain of *Leishmania tropica,* or Oriental sore, provoked a specific reaction in the bearers of our (Brazilian) type of *Leishmania.* This argues in favor of the unity of the alleged species.

8. We have not yet had the opportunity to produce the cutaneous reaction in patients cured of leishmaniasis.

BISMUTH SALICYLATE IN EXPERIMENTAL RABBIT SYPHILIS

A STUDY OF TOXICITY, ABSORPTION, ELIMINATION AND SPIROCHETICIDAL POWER *

O. M. GRUHZIT, M.S., M.D.

DETROIT

A great number of research workers in this country and abroad are devoting their time to finding new and better antisyphilitic drugs. Recently, Sazerac and Levaditi [1] demonstrated spirocheticidal activity of bismuth in experimental and clinical syphilis. Fournier and Guenot [2] followed the initial reports of Sazerac and Levaditi with extensive clinical observations on 200 syphilitic patients. Since these reports the literature abounds with reports of favorable clinical action of bismuth in the treatment of syphilis.

In this country, McCafferty,[3] Pardo-Castello [4] (Cuba), Hopkins,[5] and Klauder [6] have presented clinical and experimental findings. In France, Sazerac and Levaditi,[1] Levaditi,[7] Fournier and Guenot,[2] and in Germany, Kolle,[8] Bieder,[9] and Giemsa [10] have given extensive reviews of the literature as well as their own clinical and experimental findings.

The use of bismuth in the treatment of syphilis by Masucci [11] dates back to 1899. Syphilitic lesions of mouth, pharynx and larynx were

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* From the Medical Research Laboratories, Parke, Davis & Company.

1. Sazerac, L., and Levadidi, C.: Traitement de la syphilis par le bismuth, Compt. rend. Acad. de sc. **173**:338, 1921; Action de certains derives du bismuth sur la syphilis **173**:1201, 1921.

2. Fournier, L., and Guenot, L.: Action therapeutique du bismuth entant gue corps simple, dans la syphilis humaine **86**:908, 1922.

3. McCafferty, L. K.: Bismuth in the Treatment of Syphilis, Arch. Dermat. & Syph. **8**:469 (Oct.) 1923.

4. Pardo-Castello, V.: The Value of Bismuth Salts in the Treatment of Syphilis, Arch. Dermat. & Syph. **7**:586 (May) 1923.

5. Hopkins, J. G.: Bismuth in the Treatment of Syphilis, Arch. Dermat. & Syph. **7**:745 (June) 1923.

6. Klauder, J. V.: Bismuth in the Treatment of Syphilis, Arch. Dermat. & Syph. **7**:721 (June) 1923.

7. Levaditi, C.: Le bismuth dans le traitement de la syphilis, Paris, Masson et Cie, 1924.

8. Kolle, W.: Die Chemotherapie tische Studien über Wismut, Med. Klin. **20**:1097, 1924.

9. Bieder, H.: Zur Wismut Behandlung der Syphilis, München. med. Wchnschr. **71**:1275, 1924.

10. Giemsa, G.: Die Chemotherapie der Syphilis durch Wismut verbindungen, München. med. Wchnschr. **41**:452, 1922.

11. Masucci: Rassegna intern. delle Malattie del naso 1889, quoted from Levadiiti · La bismuth dans le traitement de la syphilis, Paris, 1924.

treated with bismuth oxy-iodid. Reynolds [12] employed bismuth oxy-iodid in treatment of chronic ulceration, with good results. Balzer [13] in 1889 first expressed definite ideas that bismuth possesses equal therapeutic value with mercury. However, the high toxicity of ammonium bismuth citrate which he used prevented its general adaptation in the treatment of human patients.

Sauton and Robert [14] demonstrated spirocheticidal activity of bismuth in *Spirochaeta gallinarum*, an infection of chickens. Kolle and Ritz [15] failed to produce a therapeutic effect on spontaneous syphilis in rabbits (*Spirochaeta cuniculi*) by intravenous injection of colloidal bismuth. Sazerac and Levaditi,[1] impressed by the work of Sauton and Robert, undertook further study of bismuth on experimental syphilis. As a result of this work, bismuth has become closely linked with the treatment of syphilis, and hope is entertained of better clinical success.

In their initial work, Sazerac and Levaditi [1] reported observations on the toxicity of bismuth salts of citrate, lactate, subgallate and potassium tartrobismuthate, and found that intravenously the soluble salts were too toxic. Klauder [6] compared potassium sodium tartrobismuthate, potassium tartrobismuthate and bismuth tri-oxid and found that intravenously the soluble salts were contraindicated.

In this country, the antisyphilitic and experimental work has been confined mostly to the tartaric acid salts of bismuth, and no particular effort has been given to study other insoluble compounds. With this in view, bismuth salicylate was taken as a representative of the insoluble type of bismuth salts for a thorough study to determine its adaptability in the treatment of syphilis.

Bismuth salicylate or bismuth subsalicylate—$C_6H_4(OH)COOBiO$—contains about 58.5 per cent. of bismuth, and is an odorless, tasteless, white amorphous or crystalline powder almost insoluble in cold water. It is partly soluble, with decomposition, in weak acids. It was first used by Greco and Muschietti.[16] Herzog [17] states that bismuth salicylate produced no kidney lesion, gingivitis or stomatitis, also that it did not produce pain or infiltration at the site of injection. In this country,

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12. Reynolds, A. S., quoted from J. Pharmacy **58**:599, 1886.

13. Balzer, N. F.: Experience sur la toxicite du bismuth, Compt. rend Soc. de biol. **41**:537, 1889.

14. Sauton, A. E., and Robert, B.: Action du bismuth sur la spirillose des poules, Ann. de l'Inst. Pasteur. **30**:261, 1916.

15. Kolle, W., and Ritz, H.: Experimentalle Untersuchungen über die Wilkung des Silbers und seiner Verbendungen auf die Kaninchen Syphilis, etc., Deutsche. med Wchnschr. **45**:481, 1919.

16. Greco and Muschietti: Semana med. **51**, 1922, quoted from Levaditi: Le bismuth dans la traitement de la syphilis, Paris, 1924.

17. Herzog, F.: Pharmakologie der Wismut präparate in Bezug auf die Therapie der Lues, Med. Klin. **20**:1333, 1924.

Ballenger and Elder [18] used bismuth salicylate in 1922, suspended in olive oil together with camphor and creosote, "to lessen the pain and render the technic less exacting." The same vehicle was retained throughout these studies as it is self-sterilizing, lowers the viscosity of the vehicle by 30 per cent. and besides the slight tarry odor possesses no objectionable features.

TOXICITY

The toxicity to normal and syphilitic rabbits was determined by injecting graduated doses of bismuth salicylate deep into the muscles of the back. The change in the weight of the animals was used as a measure of toxicity to the test animals. The weight was recorded in the morning before feeding the animals. The animals remained under observation from forty-four to 120 days. Figure 1 represents the curves of weight changes from the original weight at the time of injection. Curve *A* indicates changes in the weight of a rabbit following an injection of 2 gm. per kilogram. It is noted that the rabbit from the start began to lose weight, and died at the end of fifty-eight days.

Curve *B* represents the change in weight following the injection of 1 gm. of bismuth salicylate per kilogram of body weight. For seventy-four days following the injection the rabbit's weight remained about stationary. The rabbit developed intercurrent disease and died at the end of 102 days. The dosages for the foregoing two rabbits were 1,000 and 500 times, respectively, larger than the human therapeutic dose of bismuth salicylate. If the weight changes indicate the possible degree of toxicity, then 1 gm. of bismuth salicylate per kilogram represents a tolerated dose and 2 gm. a toxic dose.

Curves *D* and *C* represent the weight changes in rabbits receiving 85 and 65 mg. respectively of bismuth salicylate per kilogram of body weight or about from forty to thirty times the human therapeutic dose. The former shows steady gain, while the latter at first shows loss and then gain in weight.

Curve *E* represents the weight changes in a syphilitic rabbit that received ten doses of bismuth salicylate of 5 mg. each. The weight was decreasing slowly. After discontinuation of the treatment, there was some gain in weight; the rabbit, however, died at the end of sixty-nine days from the combined effect of bismuth and severe purulent bronchopneumonia.

Curve *F* represents the average weight changes in five syphilitic rabbits treated with 2 mg. doses of bismuth salicylate per course of ten treatments. During the treatment the weight remained just above normal. The rabbits commenced to gain more steadily after discontinuation of the treatment. One of these rabbits developed intercurrent infec-

18. Ballenger, E. G., and Elder, O. F.: Bismuth Salicylate in the Treatment of Syphilis, Therap. Gaz. **49**:159, 1925.

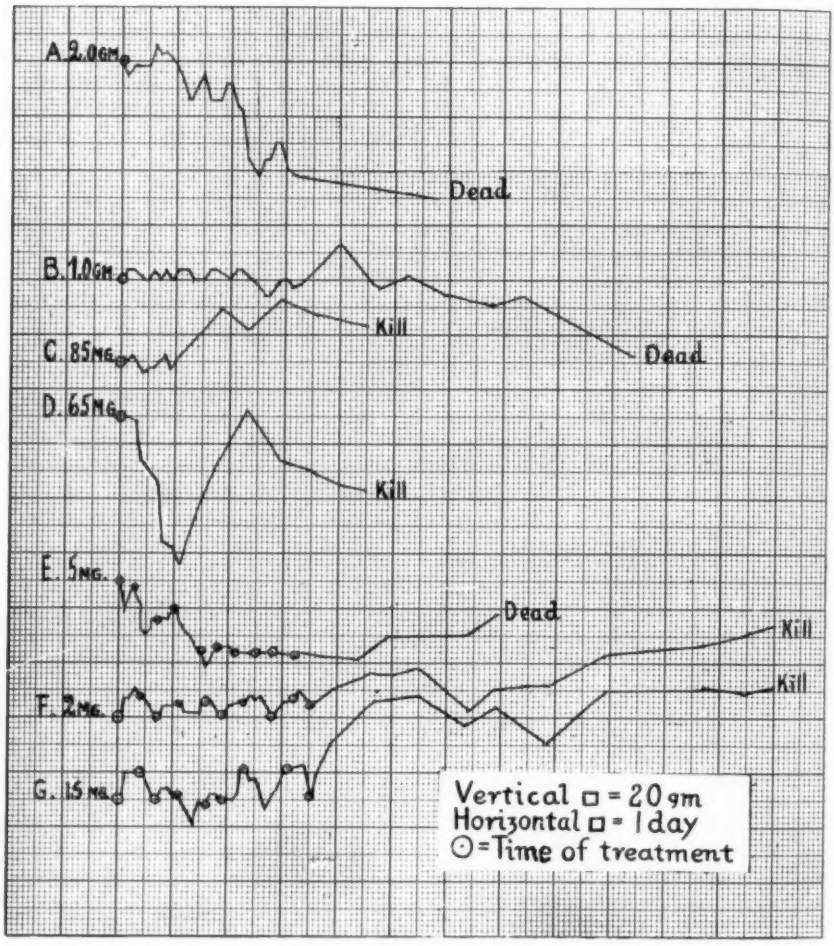

Fig. 1.—The curves represent the weight deviation from the normal weight at the time of first injection of bismuth salicylate. Curves *A*, *B*, *C* and *D* show the weight changes in rabbits receiving, respectively, 2 and 1 gm. and 85 and 65 mg. per kilogram of body weight. The curves *E* and *G* indicate the weight changes following ten injections of 5 and 1.5 mg. each per kilogram, respectively. Curve *F* represents the average changes in weight in five rabbits receiving 9 or ten injections of 2 mg. each per kilogram of body weight.

tion with a negative weight balance. This considerably reduced the average gain in weight. A slightly smaller dosage of 1.5 mg. per kilogram for a course of ten treatments given to a syphilitic rabbit produced changes in weight similar to 2 mg. per kilogram dosage. From the study of these curves, it is noted that the drop in the rabbits' weight was in no way synchronous with the injections; however, marked gain in weight occurred after the completion of a course of injections.

In summary, it appears that a dose of 1 gm. per kilogram of bismuth salicylate is not injurious when injected intramuscularly. A larger dosage impairs the health of the experimental rabbits. A therapeutic dose of from 0.5 to 3 mg. per kilogram in syphilitic rabbits produces no noticeable loss of weight during or after a course of treatment.

ABSORPTION

The rate of absorption of an insoluble bismuth salt is essential to the process of estimation of dosage and the complications which may arise. In general, absorption is more rapid from an active muscle tissue than from a muscle little used. This is probably explainable on the basis that insoluble compounds like bismuth salicylate are rendered soluble with decomposition by acids liberated during the activity of a muscle.

In this study one human dose of bismuth salicylate, potassium tartrobismuthate, an organic arsphenamin preparation and bismuth oleate was injected into the rabbit's spini recti, or in the flexor muscles of the hind legs. As noted in Figs. 2 and 3, absorption was more rapid from the leg muscles than from the spini recti muscles. It was further noted that the greatest absorption took place during the first two weeks. In the second week the oil is gradually saponified with calcium soap formation, which may remain at the site of injection for a considerable time and give a false roentgen-ray shadow. This in itself is no fault of the bismuth compound, but of the oil vehicle. Beinhauer and Jacob [19] by roentgen-ray studies conclude that there is a noticeable difference in absorption of bismuth salicylate as compared with the Neo-trepol and potassium tartrobismuthate. This is not indicated by our roentgen-ray and histologic studies.

Cole and his associates [20] state that the metallic bismuth was not absorbed in 150 days and that another preparation of bismuth in oil showed no absorption in forty-four days, while bismuth salicylate

19. Beinhauer, L. G., and Jacob, F. M.: The Relative Absorption and Therapeutic Efficiency of Some Bismuth Preparations, Am. J. Syphilis **9**:213, 1925.

20. Cole, N. H.: Farmen, H. L., and Miskdjian, H.: The Intramuscular Absorption of Some Insoluble Bismuth Compounds as Revealed by the X-ray, read at the meeting of the American Dermatological Association, Washington, D. C., 1925, to be published.

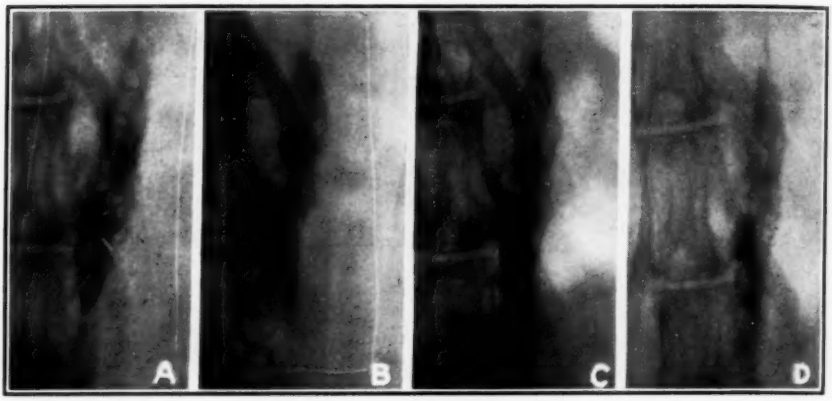

Fig. 2.—Absorption of bismuth salicylate from a passive muscle of the back. The roentgenograms were taken following the injection, and subsequently on the thirtieth, forty-eighth and sixty-sixth day. The dosage was 0.078 gm. metallic bismuth.

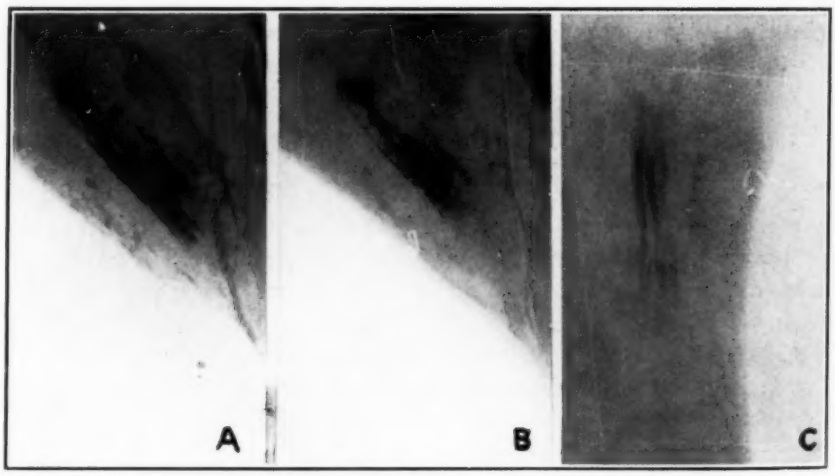

Fig. 3.—Absorption of bismuth salicylate from an active muscle of the thigh. The roentgenograms were taken following the injection and subsequently on the fifth and ninth day. The dosage was 0.078 gm. of metallic bismuth.

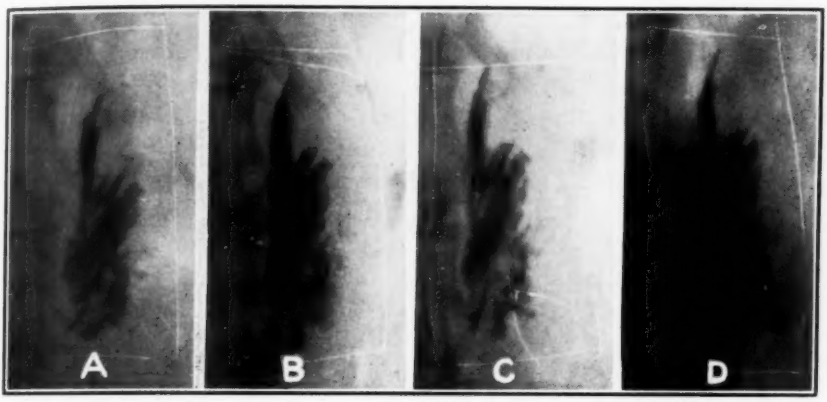

Fig. 4.—Absorption of potassium bismuth tartrate from a passive muscle of the back. The roentgenograms were taken on the first, thirtieth and fifty-first day. The dosage was 0.045 gm. of metallic bismuth.

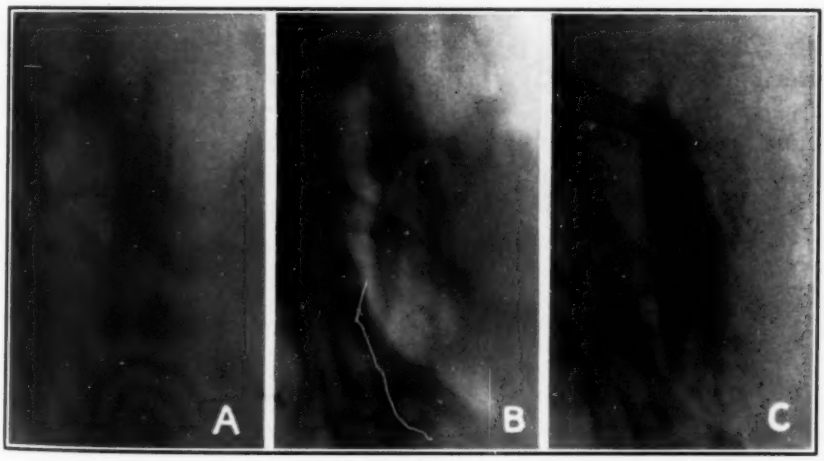

Fig. 5.—Absorption of an organic arsphenamin preparation from a passive muscle of the back. The roentgenograms were taken on the first, thirtieth, forty-eighth and sixty-sixth day. The dosage was 0.2 gm. of metallic bismuth.

showed complete absorption in ten cases in forty-five days, and it was still unabsorbed in thirty-four other cases in from fourteen to 124 days or in median of thirty days.

In the present studies the absorption of bismuth salicylate was materially hastened when injected into an active muscle of leg, as shown in Figure 3, and in forty-seven days there was only a trace of bismuth demonstrable under the microscope. Bismuth salicylate, like precipitated bismuth, remains in compact masses in proximity to the muscle tissue. A connective tissue capsule may or may not form around it. In cases in which potassium bismuth tartrate and bismuth oleate are used, necrosis of the tissues is produced which is followed by liquefaction necrosis, edema and leukocyte infiltration. In this mass bismuth is suspended in globules. Because of a large necrotic area in which the globules are spread, it may not give a roentgen-ray shadow at all. Microscopically, however, the bismuth is present.

During a period of from seven to ten weeks the difference in the roentgenograms and histologic sections of the various bismuth compounds is so slight that it does not permit one to draw further conclusions than to indicate that the compounds referred to in the foregoing are slowly absorbed and that large amounts of bismuth are present in the tissues for a considerable time.

SPIROCHETICIDAL POWER

A group of fifteen rabbits with well developed syphilitic lesions of both testes were selected. In the majority of cases the lesions consisted of a generalized orchitis; in a few cases orchitis was associated with a scrotal gumma (Rabbits 55 and 74) and in one case orchitis and chancre were concomitant (Rabbit 26). In every case the lesion contained actively motile *Spirochaeta pallida* from 50 to 2 per microscopic dark field. These rabbits were treated with bismuth salicylate in olive oil, camphor and creosote suspension. The dosage varied from 0.5 to 5 mg. of bismuth salicylate per dose. Injections were administered intramuscularly into the spini recti or into the flexor muscles of the thigh in about every three to five days intervals for from eight to eleven treatments.

Before the treatment of the rabbits with bismuth salicylate a fluid was aspirated from one testis and examined for the presence of *Spirochaeta pallida*. This process was repeated every twenty-four hours until the spirochetes disappeared from the lesion; then the other testis was aspirated. As a rule no spirochetes were found in the second testis when the first showed none. In Table 2, the average result of examinations of both testes are reported. It is noted from these results that a single dose of 5 mg. per kilogram rendered the lesion free from spirochetes in forty-eight hours.

A dose of 3 mg. per kilogram rendered the spirochetes nonmotile, but was not able to destroy them in the lesion until after the third treatment. This, however, may have been due to the fact that the rabbit had a gumma in the wall of the scrotum, and in this gumma the spirochetes persisted while the body of the testis was free from spirochetes after the first treatment. A dose of 2 mg. per kilogram in two rabbits rendered the spirochetes nonmotile after the first treatment in from forty-eight to seventy-two hours. A second treatment with 2 mg. per

TABLE 1.—*Bismuth Salicylate, Dosage, Number of Treatments and Time of Lymp Node Transfers*

Rabbit	Mg. per Kg.	Days Treated											No. of Treatments	Lymph Node Transfer
32	2.0	0	3	7	11	16	19	23	26	29	33	..	10	On 43d day
55	3.0	0	3	7	11	—	19	23	26	29	33	..	9	On 34th day
22	5.0	0	3	7	11	16	19	23	26	29	33	..	10	On 43d day
12	2.0	0	4	7	11	15	18	22	26	30	32	..	10	On 49th day
33	2.0	0	4	7	11	15	18	22	26	30	32	..	10	On 49th day
66	1.5	0	4	7	11	15	18	22	26	30	32	..	10	On 49th day
88	1.0	0	4	7	11	15	18	22	26	30	32	..	10	On 49th day
20	2.0	0	4	7	11	15	18	22	26	30	32	..	10	On 52d day
17	2.0	0	4	7	11	15	18	22	26	30	32	..	10	On 52d day
51	2.0	0	4	7	11	15	18	22	26	30	32	..	10	On 52d day
67	2.0	0	4	7	11	14	18	22	—	33	37	..	9	On 58th day
31	1.0	0	4	7	11	14	18	22	—	33	—	..	8	On 39th day
74	0.5	0	4	7	11	14	18	22	29	33	—	41	11	On 58th day
62	0.5	0	4	7	11	14	18	22	29	33	—	41	11	On 58th day
26	2.0	0	3	7	12	16	19	23	27	31	36	..	10	On 56th day

TABLE 2.—*The Effect of Bismuth Salicylate on Spirochaeta Pallida in Experimental Rabbit Syphilis*

Rabbits	Mg per Kg.	Spirochaeta pallida, Days Examined															
		0[t]	2	3	4[t]	5	7[t]	9	11[t]	13	15	18	21	65	92	104	
32	2.0	4+	4+	+[t]	..	—	—	—	—	..	—	—	..	—	—	—	..
12	2.0	4+	4+	..	4+	2+	—	—	—	..	—	..	—	33—	49—	65—	77—
33	2.0	4+	4+	..	+[0]	+	—	—	—	..	—	..	—	—	—	—	—
20	2.0	4+	4+	..	4+	—	—	—	—	..	—	..	—	—	—	—	—
97	2.0	4+	4+	..	+	+	—	—	—	..	—	..	—	—	—	—	—
67	2.0	4 d	....	..	+	—	+	..	—	—	..	..	—	—	57—	..	..
26	2.0	4+	+	+[t]	—[0]	—	—	..	..	..	16[t]	..	..	..	..	..	..
55	3.0	4+	—	+[t]	..	+	—	+	—	..	—	—	..	..	..	..	..
22	5.0	4+	—	—[t]	..	—	—	—	—	..	—	—	..	65—	..	..	..
66	1.5	4+	4+	..	4+	4+	—	—	—	..	—	—	—	33—	49—	65—	77—
88	1.0	4+	4+	..	4+	4+	—	—	—	..	—	—	—	—	—	—	—
31	1.0	4+	..	..	4+	..	—	—	—	—	..	..	..	20—	..	..	..
74	0.5	4+	..	..	4+	..	4+	..	4+	4+[t]	4+	+[t]	..	22[t]—	28—	32—	57—
62	0.5	4+	..	..	4+	..	—	..	—	—	14[t]	t	..	22[t]—	32—	57—	..

[t] indicates days treated; [0], no treatment; 4+, actively motile Spirochaeta pallida; +, Spirochaeta pallida few and nonmotile; —, Spirochaeta pallida not found.

kilogram eliminated the spirochetes from the lesion in all (seven rabbits), but one rabbit in from four to eight days, or on an average of about six days.

No material deviation from the results shown in Table 2 was noted with doses as low as 0.5 mg. per kilogram except in encapsulated gumma of the scrotal wall (Rabbit 74). In generalized orchitis the dose of 0.5 mg. per kilogram appeared as efficient as that of 1, 1.5 or 2 mg. per kilogram.

The spirocheticidal value and the healing effect of bismuth salicylate on the lesions are well illustrated in Rabbit 26, Fig. 6. *A* represents testes before treatment. Surface secretions showed under dark-field illumination from ten to fifteen actively motile spirochetes per field. The diameter of the induration on the left measured 2.45 cm. and the ulcer 1.45 cm. The left testis induration and ulcer measured, respectively,

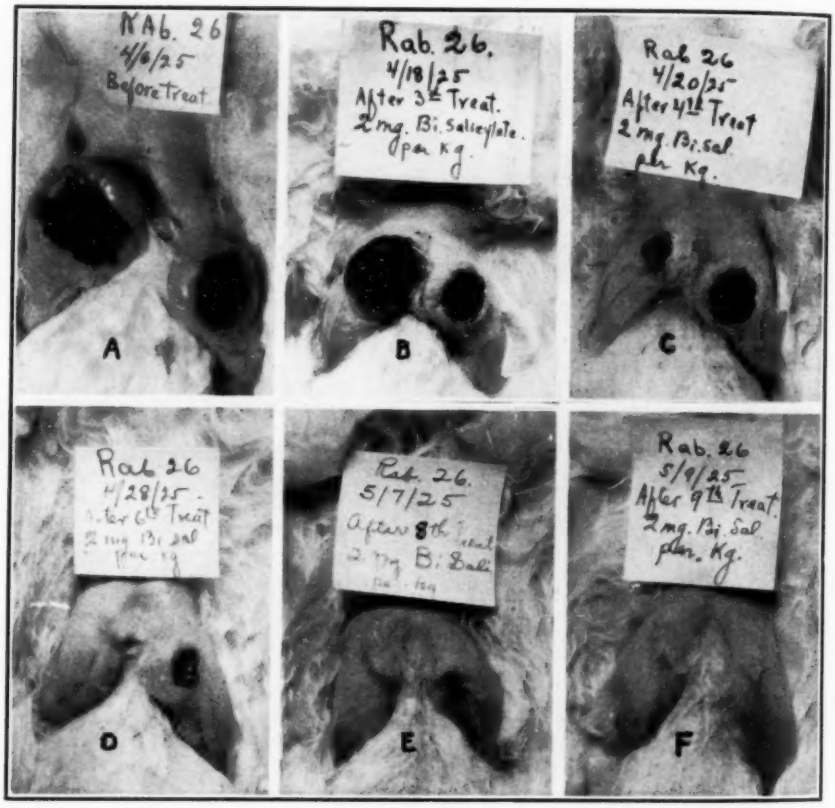

Fig. 6.—The changes in the lesion under treatment with bismuth salicylate. *A*, before treatment with activity motile spirochetes *B*, *C*, *D*, *E* and *F*, respectively, after third treatment on twelfth day, fourth treatment on fourteenth day, sixth treatment on twenty-second day, eighth treatment on thirty-fifth day and ninth treatment on thirty-seventh day. The left testis was normal in seventeen days, and the other in thirty-three days, with a cumulative dosage of 10 and 18 mg. of bismuth salicylate per kilogram, respectively.

1.6 and 0.7 cm. across. Both lesions were secondarily infected, and pus pockets penetrated deep between the induration and the skin. Equal extent and severity of the lesions would be hard to find in human patients. A single injection of 2 mg. of bismuth salicylate rendered the spirochetes nonmotile in forty-eight hours. In seventy-two hours only

an occasional nonmotile granular spirochete was present. In ninety-six hours or the day following the second treatment, no spirochetes were found in either testis.

The involution of the lesion was slower. On the seventh day the induration of the left testis was about half in size (1.1 cm.), while the lesion on the right testis showed little or no change. On the twelfth day the induration on the left was entirely gone. The right side showed slight change. The lesion on the left was entirely healed seventeen days after the fifth treatment; the lesion on the right testis was healed thirty-three days after the ninth injection of bismuth salicylate.

The process of involution occurred gradually. The improvement in the chancres, however, was noticed following the first injection, but no phenomenal or sudden changes were induced. The secondary infection undoubtedly was a factor in retarding the healing. The disappearance of the spirochetes, the regression and the healing of the lesions distinctly indicate the value of bismuth salicylate as an antisyphilitic agent.

CURATIVE VALUE

After a course of treatment the rabbits were allowed to rest for a period varying from one week to three weeks. At the end of this time the popliteal nodes were excised, emulsified and injected into the testes of healthy, normal rabbits. Both the treated rabbits and those from which lymph node transfer was made were kept under observation, the former for recurrence of the lesion and the latter for development of a lesion. At the end of about ninety days, the animals were killed, and the testes were excised and examined histologically for pathologic changes. If in sixty days the rabbits into which the lymph node transfer was made had not manifested formation of a lesion, as a rule, a second popliteal lymph node transfer was made to another normal rabbit's testes. If a rabbit from which a lymph node had been transferred died from intercurrent disease before the expiration of ninety days of observation, the popliteal glands from the first transfer were excised and transferred into a second normal rabbit's testes. This precaution was necessary as Pearce and Brown's [21] work with lymph node transfer as an index of measure of curative value had not been thoroughly checked over. However, since this work was completed a recent publication on the subject of lymph node transfer by Chesney and Kemp [22] leaves no doubt of its reliability.

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21. Pearce, L., and Brown, W. H.: A Study of the Relation of Treponema Pallidum to Lymphoid Tissue in Experimental Syphilis, J. Exper. Med. **35**:39, 1922.

22. Chesney, A. M., and Kemp, J. E.: Studies in Experimental Syphilis, J. Exper. Med. **42**:33, 1925.

In these experiments the smallest dose employed (0.5 mg.) per course of eleven treatments was sufficient to render the lymph nodes innocuous to a normal rabbit. Not one of the normal rabbits receiving injections of lymph node emulsion from treated rabbits developed a lesion, and in none of the treated rabbits was noted recurrence of the lesion or reappearance of spirochetes.

EFFECT UPON THE KIDNEYS

Kollert and his associates [23] observed kidney lesions in rabbits poisoned with sodium potassium tartrobismuthate. The changes were similar in nature to those of mercury poisoning. Lucke and Klauder [24] found that toxic doses of sodium potassium, potassium tartrobismuthate and bismuth tri-oxid produced degeneration of the kidneys and liver, ranging from severe cloudy swelling to extreme necrosis and calcification. In their opinion, the foregoing bismuth compounds exerted greater nephrotoxic than hepatotoxic action. No studies have been made of the effect of tolerated and therapeutic dosages on the various organs. With this in view, histologic examination of the kidneys, liver and other organs was made on normal and syphilitic rabbits.

Two grams of bismuth salicylate per kilogram of body weight caused the death of a rabbit in fifty-eight days. The kidneys presented a number of old scars in the cortex and medulla. The greatest portion of tubuli contorti was obliterated and necrotic. The glomeruli, however, remained unaffected. No calcium deposits were found. The liver presented severe fatty degeneration with a number of necrotic cells. At death the site of injection contained a large amount of bismuth.

One gram single dose of bismuth salicylate per one kilogram of body weight in 102 days produced no calcification in the kidneys. The tubuli contorti cells showed a mild degree of cloudy swelling. The tubuli recti cells were hydropic. The nuclei, however, stained normal. The liver cells indicated a mild degree of fatty degeneration and cloudy swelling. The gallbladder epithelium appeared normal. Few eosinophils were scattered through the liver tissues. The injury to the kidneys was comparatively slight. The liver cells manifested in degree more degenerative changes than the kidneys. At necropsy bismuth was present at the site of injection.

A single dose of 65 to 85 mg. per kilogram of body weight at the expiration of from thirty to forty-five days had affected the organs

23. Kollert, V.; Strasser, U., and Rosner, R.: Trepol und Niere, Wien. klin. Wchnschr. **36**:49, 1923.

24. Lucke, B., and Klauder, J. U.: Histological Changes Produced Experimentally in Rabbits by Bismuth, Pharm. & Exper. Therap. **21**:313, 1923.

differently in different animals. Some rabbits' kidneys manifested a considerable amount of calcium deposits with severe tubular epithelium degeneration, while in other rabbits the injury was slight and no calcification was noted. The liver cells, however, presented in every case a definite but not a severe degree of fatty degeneration and cloudy swelling.

Repeated injections into syphilitic rabbits of quantities of bismuth salicylate varying from 0.5 to 3 mg. per kilogram of body weight for a course of from eight to eleven treatments produced no microscopic changes in the kidneys or liver at the end of one or two months.

One syphilitic rabbit was given ten injections of 5 mg. per kilogram of body weight—a total of 50 mg. per kilogram of bismuth salicylate. This rabbit developed severe purulent bronchopneumonia, and death resulted from the combined effect of pneumonia and bismuth. The kidneys and liver of this rabbit presented severe degenerative changes, however, without calcium deposits.

Histopathologic study of rabbits's kidneys and liver, therefore, indicates that a single injection of 2 gm. per kilogram produces severe pathologic changes in rabbits, resulting in death. A single injection of 1 gm. per kilogram usually shows only slight injury to all organs; in some rabbits no pathologic changes were noted. A smaller dosage of from 0.5 to 3 mg. per kilogram administered to syphilitic rabbits for from eight to eleven treatments showed no histopathologic changes in the kidneys or liver.

EFFECT OF BLOOD UREA NITROGEN

It is generally thought that a kidney injury is invariably associated with urea retention in the blood stream. This principle, therefore, was utilized in the study of the effect of bismuth salicylate on the kidneys to make doubly sure as to its low toxicity and to determine a safe dosage. For this purpose, three normal, healthy dogs were selected and repeatedly examined for the presence of albumin in the urine and retention of blood urea nitrogen. Following this preliminary examination, the dogs received injections of bismuth salicylate. A dog weighing 16 kilograms received one human dose of 0.135 gm. of the substance deep in the muscle of the thigh. A second dog weighing 17 kilograms received injections with three times this amount. A third dog weighing 17 kilograms received repeatedly intramuscularly a dose of 2 mg. per kilogram, or a total of 34 mg. per dose, twelve times during a period of sixty days.

The first dog received per kilogram, therefore, about five and the second dog about twelve times the initial human dose. The third dog received cumulatively as much as either dog individually, and therefore, served at the same time as a control to the first two dogs.

When the blood was drawn for analysis, the dogs as a rule were placed on very low protein intake or received no food for three days previous to it. This procedure, according to Korenchevsky [25] in his studies of protein metabolism, gave the best and most uniform results. The blood urea nitrogen determination was made according to Karr's [26] method.

The blood urea nitrogen determinations were carried for over a period of six months. The results are summarized in Figure 7 in the form of curves. The initial point of the curves represents an average normal blood urea nitrogen content in four different analyses. Curves *A* and *B* represent changes in blood urea nitrogen from dogs treated with a single dose of 135 and 405 mg., respectively. Curve *C E* represents a

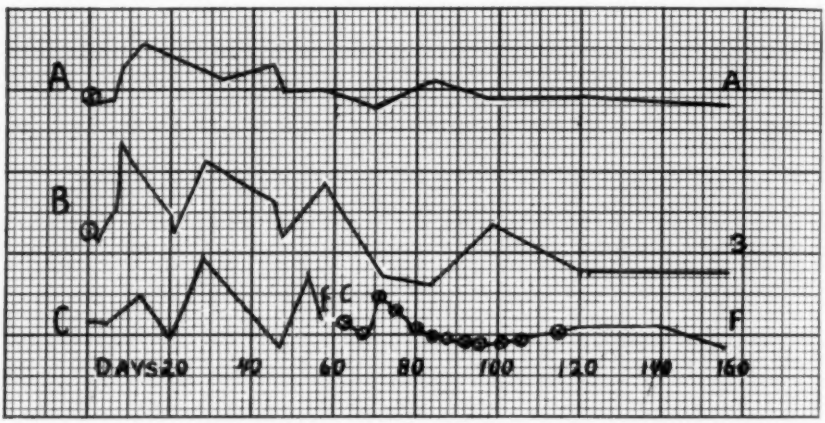

Fig. 7.—Blood urea nitrogen changes under treatment with bismuth salicylate with single doses of 0.135 (*A*) and 0.405 gm. (*B*). Curve *C D* shows normal blood urea nitrogen in Dogs C and C E, the same dog under twelve injections of about four day intervals with a dose of 2 mg. per kilogram; the total dosage is 0.408 gm.

normal variation of blood urea nitrogen of the third dog before treatment with bismuth salicylate, and the continuation of it as *C D* shows the blood urea nitrogen content following the treatment of the same dog with twelve injections totaling 408 mg. The circles indicate the time of injection. The normal average blood urea nitrogen content of Dog A was about 9.3 mg. per hundred cubic centimeters of blood. In Dog B the average was about 12.8 mg. In Dog C the blood urea nitrogen

25. Korenchevsky, V.: Castration Influence on Nitrogen and Gaseous Metabolism, Brit. Exp. Pathology **6**:21, 1925.

26. Karr, W. G.: A Method for the Determination of Blood Urea Nitrogen, J. Lab. & Clin. Med. **9**:329, 1924.

varied between 8.4 and 20 mg. per hundred cubic centimeters of blood, an average of about 12.6 mg. It is noted from the curves that there was a slight rise of blood urea nitrogen after the sixth day; however, the variations were within the limits of variations of the normal dog.

Presenting the blood urea nitrogen changes in periods of twenty days, with 4, 2, 3, 3, 2, 1, 1 and 1 determination for each period, it is noted that the variations of blood urea nitrogen content are in the range of experimental error and differ only slightly from the normal content. This is well shown in the case of Dog C. The first four figures represent normal blood urea nitrogen content, while the remaining figures were obtained after injection with bismuth salicylate. The blood urea nitrogen content in this dog remained stationary or slightly decreased. From these comparisons it is strongly indicated that bismuth salicylate when injected intramuscularly in from 5 to 12 times larger single doses or when injected with the same dosage per kilogram as used in human beings per a course of twelve injections shows no increase of blood urea nitrogen, and indirectly therefore does not injure the kidneys.

TABLE 3.—*Urea Nitrogen Content of the Blood*

Dog	Normal Blood Urea Nitrogen per 100 C.c. of Blood	Blood Urea Nitrogen in Periods of 20 Days								
		1st	2d	3d	4th	5th	6th	7th	8th	9th
A	9.3 mg.	11.10	12.30	10.9	8.25	9.8	7.8	—	7.9	12.4
B	12.8 mg.	16.40	15.65	15.6	10.06	9.8	7.0	—	7.6	9.1
C	12.7 mg.	12.20	15.50	12.6	12.06	9.9	10.4	10.6	8.5	....

During the whole course of observations of the three dogs urinalyses for albumin were made frequently, and not in a single instance was there an indication of albuminuria.

To summarize: It is apparent from these studies that bismuth salicylate in therapeutic doses neither causes retention of blood urea nor produces kidney irritation. In tolerated doses of 1 gm. per kilogram of body weight bismuth salicylate produces slight kidney and liver injury, of which the liver injury appears more distinct than that of the kidney. In toxic doses of more than 1 gm. per kilogram the injury is severe to both the kidneys and the liver. In therapeutic doses there is neither histologically demonstrable injury to any of the organs, nor other manifestations indicating injurious effect to the experimental animals.

ELIMINATION

The same dogs used in the study of the blood urea nitrogen were utilized for the study of bismuth elimination. Dogs A and B received 135 and 405 mg. of bismuth salicylate, respectively. The third dog, C, received injections of 408 mg. of bismuth salicylate in twelve sepa-

rate doses at about four day intervals. The urine and feces were collected at first at from twelve to twenty-four hour periods. In the second and third months only weekly specimens were taken. Later specimens were taken at irregular periods.

The bismuth was not found in the urine during the first twelve hours. During the next twenty-four hours the dog receiving one human dose showed 0.35 mg. of bismuth. The dog receiving three human doses showed 0.86 mg. of bismuth in the same period. The third dog receiving only 2 mg. per kilogram, eliminated in its urine for the first seventy-two hours only 0.27 mg. of bismuth.

The bismuth elimination increased up to the fifth day, when it reached the maximum of 1.3 and 3.1 mg. of bismuth, respectively, in Dogs A and B for a period of twenty-four hours. During the second week the maximum and minimum of the eliminated bismuth per twenty-four hours fluctuated between 0.14 and 0.7 mg. During a period of twenty-six days, the average elimination in the Dogs A and B, respec-

TABLE 4.—*Bismuth Elimination* *

Dog	Bismuth Salicylate, Mg.	Bismuth, Mg.	In Urine		In Feces		Total Bismuth Eliminated, Mg.
			Mg.	Per Cent.	Mg.	Per Cent	
A	135	79.0	13.4	83.5	2.6	16.5	15.99
B	405	236.9	23.4	77.4	6.8	22.6	30.24
C	408	238.7	29.7	91.8	2.6	8.2	32.31

* Complete results on bismuth absorption and elimination will be presented fully in another paper. The bismuth determinations were made by Mr. F. H. Tendick from the Chemical Research Laboratory of Parke, Davis & Company.

tively, was 0.24 and 0.44 mg. of bismuth per twenty-four hours. At the end of three and one-half months the twenty-four hour rate of elimination in the two dogs was the same—0.24 mg. of bismuth.

Dog C received a dose of 34 mg. of bismuth salicylate in about every four days and eliminated in the urine for the first three days 0.27 mg. of bismuth. Following each successive injection the elimination rose steadily, until after the third injection it reached the maximum elimination of 1.02 mg. of bismuth per day, and before the fourth injection the elimination decreased to about 0.6 mg. of bismuth per day and never increased above this point but at times dropped to as low as 0.2 mg. irrespective of the quantity of bismuth salicylate administered.

The total amount of bismuth eliminated in the urine and the feces for a period of sixty-five days collected and analyzed, covering a period of 105 days for Dogs A and B and only sixty-five days for Dog C is shown in Table 4.

It is noted from the above summarized results that elimination of bismuth increases with the increase of dosage. The elimination is con-

siderably augmented by the frequency of administration (Dog C). This fact is brought out irrespective of the periods compared, thus at the end of 14 days Dogs A and C received equal amounts of bismuth salicylate. Dog A, receiving a single dose and Dog C four repeated injections eliminated respectively 4.9 and 6.5 mg. bismuth, while Dog B receiving thrice the above dose in a single injection eliminated in the same period of time, 11.6 mg. bismuth. The total amount of the bismuth eliminated is considerably influenced by the quantity and the frequency of bismuth administered.

COMMENT

Klauder [6] reported that the therapeutic active dose of sodium potassium tartrobismuthate in aqueous solution and in oil and potassium tartrobismuthate in aqueous solution was at least 50 mg. per kilogram. Kolle [8] states that the therapeutic active dose of sodium potassium tartrobismuthate was 5 mg. and of potassium tartrobismuthate was 6 mg. per kilogram. Hopkins [5] found that even 2 mg. per kilogram of sodium potassium tartrobismuthate in the majority of cases cleared spirochetes from the lesion in a single dose. The therapeutic active dose of bismuth salicylate is given by Kolle as being 3 mg. per kilogram, i. e., half that of potassium tartrobismuthate.

In our work a single dose of 5 mg. per kilogram of bismuth salicylate rendered the lesion free from spirochetes in less than forty-eight hours, while a single dose of 3 mg. per kilogram cleared up a generalized orchitis from spirochetes but was not able to free gummas from spirochetes. In a course of eleven injections a dose of 0.5 mg. per kilogram of bismuth salicylate produced absolute cure. A dosage of from 1 to 2 mg. per kilogram produced absolute cure in rabbits in from eight to ten doses.

The healing of a syphilitic lesion is considerably influenced by the character of the lesion, and the comparison therefore is difficult. Hopkins [5] states that 25 mg. per kilogram of sodium potassium tartrobismuthate healed a lesion in three weeks, and that 100 mg. of the same salt produced healing of the lesion in some instances in two weeks and in others in six weeks. In our cases the smaller lesions with relatively little induration healed within a week to ten days. In a case of large, extensively indurated lesions, some healed with a total of 10 mg. per kilogram in about seventeen days, while in others it took 18 mg. per kilogram of bismuth salicylate in a maximum of thirty-three days.

This would indicate that bismuth salicylate in the treatment of experimental rabbit syphilis is equal to or better than the tartrobismuthates. The optimum effective dose in a course of a treatment is from 0.5 to 1 mg. per kilogram.

Chesney and Kemp [22] have recently checked up Pearce and Brown's [21] work on the reliability of lymph node transfer as an index of a cure of experimental syphilis and lead us to believe that this method of testing is the best in evaluating the efficiency of an antisyphilitic agent. In accordance with this method, bismuth salicylate produces absolute cure in a course of eleven treatments with quantities of 0.5 mg. per kilogram, or a total of 5.5 mg. per kilogram of bismuth.

From the studies on absorption, elimination and histologic examination of the site of injections with bismuth salicylate, an organic arsphenamin preparation, potassium bismuth tartrate and bismuth oleate, it has been noted that metallic suspensions of bismuth are the least absorbed, and that no difference could be noted between the tartrate and salicylate when given in oil. This was unexpected, as the potassium salt is water-soluble. However, analysis of the commercial potassium bismuth tartrate in oil showed that in some samples 97.6 per cent. of bismuth was in water-insoluble form. Further study revealed that sterilizing in autoclave changed the soluble potassium bismuth tartrate in oil into an insoluble salt proportionally to the time of sterilization. Corfield and Adams [27] have brought out thoroughly the unstable nature of monobismuth tartrate salts under different conditions.

This undoubtedly supplies partly the true explanation as to why a water-soluble salt when mixed with vegetable oil and injected into the muscle remains unabsorbed in the tissues as long as an insoluble salt like bismuth salicylate.

The elimination of bismuth salicylate given to a dog in a single dose of 135 mg., or over four times more than the initial human dose per kilogram, over a period of 105 days averaged about 0.25 mg. bismuth per twenty-four hours. A dog receiving three times the foregoing dosage or twelve times the human dose per kilogram in a single administration eliminated during the first twenty-six days about 0.44 mg. per twenty-four hours and at the end of 105 days only 0.24 mg. of bismuth. A third dog receiving the same dose as the second but in twelve different doses, at the end of sixty-five days eliminated 0.49 mg. of bismuth per twenty-four hours and at the end of 105 days the average elimination was 0.17 mg. per twenty-four hours. The maximum at any particular time per day was eliminated by Dog B—3.1 mg. of bismuth. The elimination of bismuth never exceeded 0.7 mg. of bismuth per twenty-four hour period after the first initial rise during the first five to ten days.

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27. Corfield, B. C. E., and Adams, F. W.: Bismuth and Sodium Bismuth Tartrates, Pharmaceutical J. **57**:82, 1923.

SUMMARY

Absorption, elimination, toxicity and spirocheticidal power of bismuth salicylate has been studied.

The bismuth preparations are absorbed relatively slowly. Absorption of bismuth salicylate is more rapid than that of metallic bismuth suspensions, and is the same as that of potassium bismuth tartrate or sodium potassium bismuth tartrate.

From the total amount of bismuth eliminated, from 77 to 92 per cent. was found in the urine and from 23 to 8 per cent. in the feces.

The elimination reaches a maximum with single doses in about five days and in about ten days with fractional administration. Following the initial maximum elimination the rate of elimination becomes fairly uniform, but is greater with larger doses administered.

A fairly uniform rate of elimination increasing with increased dosage tends undoubtedly to avoid cumulative effect.

The toxicity of bismuth salicylate is comparatively low. A dose of 2 gm. of body weight per kilogram appears to be toxic, with severe injury to the kidneys and the liver. A dose of 1 gm. per kilogram appears to be readily tolerated and only a mild degree of injury was noted to the kidneys and the liver.

A therapeutic cumulative dosage of 0.5, 1, 1.5 and 2 mg. per kilogram per eight to eleven injections produced no loss of weight or histologically demonstrable lesions in the kidneys and the liver of experimental rabbits.

The gain in weight of the treated rabbits with cumulative therapeutic doses was considerably more following cessation of treatment than during the period of treatment.

Albuminuria has never been found in dogs receiving 2, 8.4 and 24 mg. of bismuth salicylate per kilogram of body weight.

Blood urea nitrogen in dogs receiving a single treatment of 8.4 and 24 mg. per kilogram, respectively, and a cumulative therapeutic dose of 2 mg. per kilogram, or a total of 408 mg., remained within the normal limits.

Bismuth salicylate in 5 mg. per kilogram rendered the lesions free from spirochetes in forty-eight hours. A 3 mg. dose produced similar results in generalized orchitis, but not on sclerotic gumma.

A cumulative dosage of 2 mg. per kilogram rendered the lesion free following the second administration in from four to seven days.

Doses of 1 and 1.5 mg. per kilogram rendered the lesion free in seven days, and 0.5 mg. doses in some cases appeared equivalent to 1 mg., in other cases it took about twenty days before the spirochetes disappeared.

Absolute cures were produced in all rabbits, even with the smallest dosage of 0.5 mg. per kilogram in a course of from eight to eleven injections as ascertained by innocuousness of lymph nodes from treated to normal rabbits.

An extensive orchitis with gumma healed in some cases with 10 mg. per kilogram in seventeen days; in other cases the lesion required 18 mg. per kilogram before it healed in thirty-three days and the testes became normal.

Bismuth salicylate possesses high spirocheticidal power and causes no pain or irritation at the site of injection; its rate of absorption appears to be better than that of metallic suspensions and is equal to that of tartrobismuthates.

GASTRIC ACIDITY IN ACNE VULGARIS

PRELIMINARY REPORT *

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AND

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PHILADELPHIA

There is a consensus of opinion that acne vulgaris is frequently accompanied by gastro-intestinal disturbances, of which constipation is most frequently recorded, and less often, so-called "dyspepsia" or "indigestion."

Two prescriptions are given in practically every textbook on dermatology for the internal treatment of this condition. One is a magnesium sulphate, ferrous sulphate, and dilute sulphuric acid mixture, and the other contains sodium salicylate, benzoate or bicarbonate.

From these prescriptions, one assumes that certain cases of acne vulgaris have a decreased and others an increased gastric acidity. While this variation has been known as a clinical fact, apparently no definite studies of gastric acidity have been made. Having this fact in mind, and hoping for improvement in certain of our intractable cases, we decided to make gastric analyses on twenty-five patients suffering from acne vulgaris. The duration of the condition varied from three months to four years. The severity of the outbreak varied from those showing only a few comedones, superficial papules and pustules to the most severe types of the condition, with numerous deep-seated papules, pustules, sebaceous cysts and a considerable amount of scarring.

Each patient was directed to abstain from food for at least six hours before the examination. A test meal, consisting of two pieces of dry toast and 250 c.c. of water, was given; the Rehfuss tube was passed, and specimens of the gastric contents were removed at fifteen minute intervals. Each specimen was titrated for the total acidity and for free hydrochloric acid, using 1 c.c. volumes of the gastric juice, one-hundredth normal sodium hydroxid, phenolphthalein indicator for the total and Topfer's indicator for the free hydrochloric acid. The findings are expressed in cubic centimeters of tenth-normal sodium hydroxid per hundred cubic centimeters of gastric juice. Ten cases gave a maximum total acidity below 50, seven between 50 and 60, four between 60 and 70, and the remaining four above 70.

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* Read at the Fifty-Eighth Annual Meeting of the American Dermatological Association, Washington, D. C., May, 1925.

Regardless of the gastric acidity, we prescribed for each of these patients a mixture containing diluted hydrochloric acid, fluid extract of cascara sagrada and tincture of nux vomica. The patients with an acidity of over 70 complained, within a few days, of burning sensations in the epigastrium. The prescription was then discontinued. The patients with a total acidity between 50 and 70 were, with one exception, not so affected. The other patients, having a total acidity below 50, were apparently benefited by the medicine, so far as their digestive function was concerned. Four of these cases, which showed certain differences from the others studied, may be cited.

REPORT OF CASES

CASE 1.—A youth, aged 18, white, had severe acne vulgaris with numerous sebaceous cysts which had lasted for three and one-half years. His total acidity reached a maximum of 76 at seventy-five minutes. The free hydrochloric acid was 55 at ninety minutes. This was fairly high acidity.

CASE 2.—A youth, aged 18, white, had mild acne vulgaris of one year's duration. His maximum total acidity was 61 at sixty minutes and free hydrochloric acid 29 at 105 minutes.

CASE 3.—A youth, aged 19, white, had acne vulgaris resembling that in Case 1, with a duration of three years. His total acidity was 40 at ninety minutes and free hydrochloric acid 20 at ninety minutes.

CASE 4.—A youth, aged 17, white, showed severe acne vulgaris of more than three years' duration. His maximum total acidity was 63 at seventy-five minutes and free hydrochloric acid 35 at seventy-five minutes.

No relation existed between the severity, type or duration of the acne vulgaris and the gastric acidity.

COMMENT

This preliminary report is fallacious in regard to arriving at definite conclusions. We feel that the investigation, so far, bears out the clinical observations. The variation in the gastric acidity in this disease should be borne in mind, and proper remedies administered.

The fact is emphasized that a gastro-intestinal study should be made in those cases which have proved intractable to the usual methods employed.

SUMMARY

1. No gastric acidity studies in acne vulgaris have been reported.

2. Twenty-five cases of acne vulgaris, varying in duration, type and severity, were examined for total and free hydrochloric acidities by the fractional gastric analysis method.

3. Ten cases showed a total acidity below 50, seven between 50 and 60, four between 60 and 70 and the remaining four above 70.

4. The acid values apparently had no relation to the duration, type or severity of the condition.

5. Patients with a low acidity were improved when given a mixture containing dilute hydrochloric acid.

6. Studies of gastric acidity should be made in those cases of acne vulgaris proving intractable to the usual methods of treatment.

DISCUSSION

DR. RICHARD L. SUTTON, Kansas City: The question of successful treatment in acne vulgaris is always with us. Some cases respond promptly to treatment, but the majority do not. The discussion on Dr. McGlasson's paper yesterday was so long and exhaustive that I did not wish to intrude on the patience of the audience, but I will mention here that in obstinate cases of acne, we have found it advisable always to check up on the blood sugar. When indicated, cutting down the sugar intake often proves beneficial.

DR. HERMANN GOLDENBERG, New York: I wish to ask whether any of Dr. Knowles' patients complained of digestive disturbances.

DR. HAROLD N. COLE, Cleveland: When we talk to the internists today we find that they are not laying so much stress on the amount of acid in the stomach. What is normal for one patient is abnormal for another, and for that reason the figures often mean nothing. In the Lakeside Hospital, Dr. M. A. Blankenhorn has been doing some work on medical students, checking this up, and has found wide variations in normal persons. It is a question whether an investigation like this will help us in arriving at a conclusion, although it is valuable to obtain all the information possible.

I hesitate to mention a single case, but eighteen months ago I had a patient with severe acne of the back, on whom I used the roentgen ray and local measures with little effect, and the patient disappeared from observation. About nine months later he stopped me on the street one day and told me that he had had his tonsils removed several months before, and had not been troubled with acne since then.

DR. CHARLES J. WHITE, Boston: Some years ago I inquired of all the patients in our skin clinic at the Massachusetts General Hospital clinic regarding their digestive troubles, and I found that seven persons out of ten complained of some digestive trouble, while in the acne and seborrheic cases the percentage reached ninety.

DR. DOUGLASS W. MONTGOMERY, San Francisco: It is rather difficult to determine the normal acidity in the individual case, as the young human animal is sturdy and so reciprocally resistant that he may have a pronounced hyperacidity without showing any direct evidence of trouble.

DR. SIGMUND POLLITZER, New York: It seems to me that these studies would have had a greater value if Dr. Knowles had examined twenty-five cases of some other common disease, e. g., scabies, in young people, as a control series with the cases of acne.

DR. J. FRANK SCHAMBERG, Philadelphia: Despite the fact that acne is a disease that has been known for many years, and many investigations have been carried out, we know little of its etiology at the present time. I am inclined to think that in speaking of acne we are speaking of more than one condition. We have the acne juvenilis, which I think is definitely associated with endocrine disturbance. We know how this occurs in young women and how the attacks are aggravated at the time of menstruation. I think another form of acne begins at a later age. I know one woman who never had

adolescent acne, who at the age of 23 developed a very stubborn form of acne. I think the acne rosacea is quite different from an etiologic standpoint from acne juvenilis. I do not believe the acne juvenilis is due to the acne bacillus. I think the organism is there, much as the staphylococcus is there, but in the acne that develops later I think the gastro-intestinal disturbances, more intestinal than gastric, are at the base of most of them. I think the condition merits restudy from the standpoint of general systemic conditions. I think we must separate one type of acne from the other, and that there are acneform conditions which should not be classified under the head of acne juvenilis.

Dr. Charles M. Williams, New York: I second Dr. Schamberg's remarks. I feel so strongly about this that I think acne rosacea should never be called acne. I think it is an entirely separate disease. Rosacea is a disease occurring in middle or late life, almost invariably associated with indigestion, and usually with gastric hyperacidity; it always seems to me, although I have made no investigation, that this is fermentative in type rather than hyperchlorhydria. In my experience the acne that develops at 23 or later is much more difficult to treat than that of early youth. In the acne associated with gastro-intestinal conditions we have not been able to obtain favorable results nearly as well as in the other type.

Dr. Frank C. Knowles, Philadelphia: What I mentioned in the paper was not in an effort to prove that acne vulgaris was entirely of gastro-intestinal origin even in the majority of cases, but to bring forward the thought that some of the cases are intractable to some, or most, of our present methods of treatment. I agree with the paper of Dr. Fox a year ago that the roentgen ray is the most advantageous means of treatment to employ in this condition, but, as I stated, there are certain cases that do not respond to roentgeno-therapy and do not respond to vaccine, and there must be some other means of cure. They do not need to be severe, but may be those cases in which there is only the oily skin, with a few papules. This study was only of those intractable cases that were not cured by other methods. You will notice in the transactions of this Association that for two or three years after the Association was founded there were cases of acne in which the gastro-intestinal symptoms in the etiology were stressed. In some of these cases some of the patients complained of gastric and intestinal symptoms, and others did not. No cases of acne rosacea were studied. The study was made simply for the few intractable cases of acne vulgaris rather than for the entire study of this disease. As Dr. Cole mentioned, it is almost impossible to get a physiologic chemist to tie himself down to the normal acidity. There is a wide variation in the views as to what constitutes normal, and that is why we mentioned only those that had a certain percentage above 50 and a certain percentage below 50 per cent. I think the majority of the profession is more inclined to give an acid in connection with roentgenotherapy rather than other treatment internally. The fact that most of us give sodium in connection with roentgeno-therapy makes this seem of benefit. It was only in the cases of intractable acne vulgaris that this condition was studied, and in which I think it was of benefit.

INTRAMUSCULAR ABSORPTION OF SOME INSOLUBLE BISMUTH COMPOUNDS AS REVEALED BY THE ROENTGEN RAY *

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It is only since 1921 that bismuth has been employed in the treatment of syphilis. Yet if one were to judge from the amount of journal space devoted to this one phase of antisyphilitic therapy, one would be inclined to think that its use was as old as that of mercury. One need only recall how numerous are the different bismuth preparations already on the market.

These preparations, following the classifications of Levaditi,[1] can be roughly grouped under four main heads:

I. PREPARATIONS CONTAINING METALLIC BISMUTH

"Neo Trepol" containing 96 per cent. of pure bismuth (finely ground up and divided) serves as an example.

II. ORGANIC SALTS OF BISMUTH

Examples of this class may be enumerated as follows:

The sodium and potassium bismuth tartrate (trepol) and other examples of this salt on the market containing from 50 to 60 per cent. of bismuth.

Bismuth salicylate with 50 per cent. of bismuth.

Bismuth succinate with 73 per cent. of bismuth.

Bismuth oleate with 20 per cent. of bismuth.

Bismuth subgallate with 50 per cent. of bismuth.

Bismuth oxybenzoate with from 58 to 59 per cent. of bismuth.

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* From the Departments of Dermatology and Syphilology and of Roentgenology of the Western Reserve University and of the Cleveland City Hospital.

* This work was done under the auspices of the Therapeutic Research Committee of the Council on Pharmacy and Chemistry of the American Medical Association.

1. Levaditi, C.: Le bismuth dans le traitement de la syphilis, Paris, Masson et Cie, 1924.

III. INORGANIC BISMUTH COMPOUNDS

Bismuth hydroxid with 64 per cent. of bismuth.
Bismuth iodid with 35.4 per cent. of bismuth.

IV. ALKALOIDAL IODOBISMUTHATES

As an example of this we might mention the preparation with quinin under the trade name "Quinby" and containing 26 per cent. metallic bismuth.

TOXICOLOGY

As far as the therapeutics are concerned, it has been known for some time that bismuth salts are dangerous in their action under certain conditions. As long ago as 1829, Kerner performed a necropsy on a man who died following the ingestion of 8 gm. of bismuth subnitrate. The patient showed a gangrenous necrosis of the digestive tract—more particularly in the stomach. Such instances kept increasing. Following the widespread use of Beck's paste, cumulative evidence began to be published leading up to the illuminating papers of Mayer and Baehr,[2] of Cabot [3] and of Higgins.[4] In most of the cases the patients showed a deposit of bismuth on the gums (bismuth line) or a more or less severe stomatitis even up to a buccal mucous membrane necrosis, nausea, emesis, gastritis and diarrhea. Albuminuria was common. Higgin's paper in 1916 reported sixty-five poisonings with twenty-four deaths. At the reading of this paper Beck admitted that of 1,100 patients treated by him, 30 per cent. showed pigmentation of the gums. Since we have begun to use bismuth in the treatment of syphilis our attention has been even more attracted to the toxicology of this drug. Lucke and Klauder [5] have experimentally produced a tubular nephritis in rabbits, and they urge the necessity of careful clinical control of all patients undergoing bismuth therapy. Koellert, Strasser and Rasner,[6] working with a sodium and potassium bismuth tartrate, compare the kidney findings in their patients to those of mercury nephritis. Levy-Bing, Gerbay and Philipeau [7] call attention to the possibility of bismuth nephritis and mentional buccal evidence of intolerance in the form of a bismuth line and stomatitis. Recently, Wotrin [8] reported a severe bismuth poisoning resulting from fifteen injections of bismuth. From

2. Mayer and Baehr: Surg., Gynec. and Obst. **15**:309-322.
3. Cabot, R. C.: Tr. Assn. Am. Phys. **27**:457-470, 1912.
4. Higgins, W. H.: J. A. M. A. **66**:648-650, 1916.
5. Lucke, B., and Klauder, J. V.: J. Pharmacol. and Exper. Therap. **21**:313-321, 1923.
6. Kollert, Strassner and Rasner: Wein. klin Wchnschr. **3**:49, 1923.
7. Levy-Bing, Gerbay and Philipeau: Ann. de mal. vener. **17**:174 (March) 1922; Rev. ann. de dermat. et. syph. **4**:748, 1923.
8. Wotrin, M. J.: Bull. Soc. franc. de dermat. et syph. **31**:27, 1924.

the standpoint of the skin, cases of generalized exfoliating dermatitis, of scarlatiniform erythema and of urticaria have been reported as concomitants of bismuth intoxications. The literature justifies us in saying that bismuth, in large enough doses, causes more or less severe inflammatory and necrotic symptoms in the digestive tract, together with congestion and degeneration with secondary cirrhosis of the liver. In the kidneys it sets up an albuminuria with desquamation of the renal epithelium even to degeneration and necrosis of the same in the tubules.

Granting that bismuth is a somewhat dangerous drug to employ in treating the human organism, surely some criteria should be evolved as to the safest, most potent and at the same time most practical preparation of this metal to be used in treating syphilis.

From the experimental work thus far carried out by Levaditi and Sazerac and by their confreres, by Kolle [9] and others, we find that bismuth is efficient as a spirocheticide. However, as a trypanosomide apparently it is not so valuable. This, as Kolle mentions, renders it rather difficult to work out a careful chemotherapeutic quotient, as has been done with the arsphenamins. From their experimental and clinical observations, most of the authors, however, seem to feel that the insoluble preparations of bismuth devised for intramuscular use are more efficient than the soluble ones devised for intravenous injections. They are certainly safer, as it has been found that the latter are ten times more poisonous. Moreover, Herzog [10] concludes that a bismuth combination to be efficient should contain 0.06 gm. metallic bismuth per injection and that in a course of six to seven weeks the patient should have received at least 1.5 gm. of metallic bismuth. This requirement at once eliminates the intravenous bismuth preparations, in which it is possible to use in one dose at the most 0.04 gm. of metallic bismuth. Serious symptoms have arisen from even 0.03 gm. At once this limits further the field of our investigation and assists us greatly in drawing deductions as to the best preparations for purposes of injection.

We have endeavored also to narrow the selection by a roentgen-ray study of the rate of absorption of some of these insoluble bismuth compounds. Many of the authors have spoken of the gradual, even absorption of insoluble bismuth salts injected intramuscularly—Levaditi in particular. He concludes that the bismuth is absorbed so slowly and in such small amounts that there is little or no danger. He even feels that the gradual giving off of the drug is a great advantage in the treatment of syphilis; and it would be if we could predict exactly the rate of absorption and elimination. We may remember that this was the old argument advanced for mercurial (gray) oil with its large

9. Kolle, W.: Med. Klin. **20**:1097, 1924.
10. Herzog, F.: Med. Klin. **20**:1333, 1924.

mercury content, even though most of the deaths from chronic mercury poisoning were due to this preparation. Myers and Corbitt,[11] working with rats, have not had the same experience as Levaditi. They found a great variability in the absorption of insoluble bismuth compounds, and they warn physicians that this brings up important problems. Kolle also mentions this. Müller, Blass and Kratzeisen,[12] using a potassium salt of bismuth tartrate, found that fifty days after the fourteenth injection of this drug they could still recover 0.006 gm. metallic bismuth per liter of urine. In another case, three months after finishing such a course the urine still showed 0.0005 gm. of metallic bismuth per liter. Fournier and Gueriot found that the urine still contained bismuth from twenty to thirty days after stopping treatment with Trepol. Wolfer[13] injected 1 c. c. (0.06 gm.) of metallic bismuth into a rabbit. In fifteen days, the roentgen-ray showed that the deposit had only partly disappeared, and in twenty-six days a shadow was still present. On the thirty-fourth day the animal was killed, and 30 per cent. of the dose was recovered from the tissues. In a second animal there was complete absorption, as far as the roentgen ray showed, in thirty-seven days; and in a third, after twenty-three days a shadow still was present. It is true that these experiments were on rabbits and not on persons. Veillet[14] reports that roentgenographic shadows like those of a fan are present from two to three months after an injection of bismuth oxid. Kolle found that there was one group of bismuth salts which resembled lead in their absorption. Thus bismuth sulphid injected into a rabbit, roentgenographically was positive eleven weeks later and a deposit of bismuth carbonate five months late. Recently Beinhauer[15] reported roentgenographic results of his study of a single bismuth injection of the following salts with time required for their absorption: iodobismuthate of quinin, four weeks; Bicreol, Neotrepol (metallic bismuth), five weeks; Bismudol (Pheyl formitate of bismuth), six weeks; potassium bismuth tartrate, eight weeks; bismuth salicylate slight, nine weeks. The author's conclusion was that relatively free metallic bismuth is more readily absorbed and that the cumulative action of bismuth should always be kept in mind.

Our results do not correspond entirely with the literature, but on the whole there is not a great deal of variance.

In studying the absorption of these insoluble bismuth compounds we have been hampered in different ways—all of which had a tendency to render more difficult the drawing of definite conclusions. For

11. Myers, C. N., and Corbitt, H. B.: Am. J. Syphilis **8**:578-594, 1924.
12. Müller, Blass and Kratzeisen: München. med. Wchnschr. **20**:625-627, 1923.
13. Wolfer, P.: Schweiz. med. Wchnschr. **3**:703-705, 1922.
14. Veillet, M. L.: Bull et mém. Soc. méd. d. hôp. de Paris **41**:35-36, 1923.
15. Beinhauer, L. G.: Pittsburgh Med. Bull. March 28, 1925, p. 9.

example, some patients would leave the hospital against advice and before they had been followed long enough. Now and then plates were unsatisfactory. However, through the data we are reporting we believe that we have sufficient evidence at hand to draw definite conclusions.

TECHNIC

Our injections were made into the lumbar region as follows: No. 1 to the right of the fourth lumbar vertebra deep into the muscle; No. 2 to the left of the fourth lumbar vertebra; No. 3 to the right of the first lumbar vertebra; No. 4 to the left of the first lumbar vertebra. By this technic we were enabled to follow four injections on one patient. Also it meant less patients to watch, less patients to lose, and was of course a great saving in roentgenograms.

In a previous roentgen-ray study made on mercury absorption, it was found that lumbar absorption was somewhat slower than gluteal, probably due to less muscular massage of the deposit. However, this would make no material difference in the relative absorbability of the different compounds.

METALLIC BISMUTH

We followed only two patients that received injections with a finely divided preparation of metallic bismuth suspended in a vegetable oil, which was kindly furnished us by Burroughs Wellcome & Co. Roentgenograms showed the bismuth as standing out sharply in the form of metallic globules. One of these patients could be followed for only forty-four days; the other patient received two injections, which are still unabsorbed after 150 and 143 days. None of the injections showed visible evidence of absorption. Eight plates were used on one injection, ten on another and twelve on the third.

BISMUTH OLEATE

Nine patients received injections of this preparation carefully prepared for us by our chemist at Lakeside Hospital. It was made up in a strength of 20 per cent. metallic bismuth in a vegetable oil. We found that the bismuth oleate injections spread out like a fan at the injected point and remained practically inert—and always somewhat difficult to see. A mean of five plates per patient were taken with extremes of three and ten. In no case did we note visible absorption, although patients were followed for the following number of days with twenty-five different injections: 12, 15, 15, 16, 19, 19, 19, 23, 23, 24, 26, 26, 28, 29, 31, 34, 38, 40, 44, 47, 50, 55, 55, 63, 68—extremes of 12 and 68 days and a median of 26 days. Eight additional injections were worthless because of the plates. We are of the opinion that if we could

have followed our patients longer we would still have found the deposits unabsorbed. Our bismuth oleate was employed in a 10 per cent. suspension in a dose of 1 c. c. or 1.5 c. c. every four days.

BISMUTH AND OXYBENZOIC ACID

There is a secret preparation of bismuth and oxybenzoic acid widely used in Germany under the trade name of "Bismogenol." Unfortunately, we lacked the material for more than two injections followed by five and six plates, respectively. The deposits showed little or no absorption after forty and forty-four days. It is true criticism might be raised as to paucity of data with this preparation. These two injections showed a phenomenon already spoken of by Wolfer, i. e., the fact that some bismuth salts when injected change their character to that of metallic bismuth. Both of our "Bismogenol" injections showed up at first as a somewhat indistinct mass in the tissues. As the deposit became older the injections roentgenographically appeared as sharply defined, large, rounded globules having the same appearance as injections of metallic bismuth or metallic mercury.

BISMUTH SALICYLATE

This salt has been highly recommended by Herzog because of its freedom from danger, in his opinion, and because of its therapeutic efficiency and high bismuth content. For this work we used a preparation kindly furnished us by Parke, Davis & Co. It is suspended in olive oil. It seemed to be efficient as an antisyphilitic and was therefore thoroughly studied, being used on sixteen patients with a total of forty-four injections. Forty-nine plates were used with a median of five plates and extremes of two and nine plates per injection. The dose of the drug employed was 1 c c. of a 10 per cent. suspension, giving a dose of 0.05 metallic bismuth per injection. The bismuth salicylate roentgenographically appears as a blotch which is distinct and well defined—even more so than the mercuric salicylate. In five instances we noted complete absorption in 28, 42, 45, 50 and 52 days; extremes of 28 and 52 days, and a median of 45 days, while in five other instances the salicylate had disappeared between 45 and 54 days, 45 and 49 days, 18 and 32 days, 45 and 108 days, and 34 and 96 days. These unfortunate discrepancies occurred because patients left the hospital and forced us to look them up. Probably a medium of plus 45 days for the patients would be low. In thirty-four other instances it was not absorbed in the following number of days: 14, 18, 18, 21, 21, 22, 22, 22, 24, 25, 25, 26, 27, 27, 28, 28, 29, 29, 30, 31, 33, 34, 34, 36, 37, 38, 40, 47, 48, 50, 74, 124—extremes of 14 and 124 days and a median of 29 days. In four instances, the plates were worthless.

POTASSIUM BISMUTH TARTRATE

For our preparation of this drug we are indebted to the Dermalogical Research Laboratories. It was employed in a 10 per cent. suspension in vegetable oil in a dose of 1 c. c. giving approximately 0.06 metallic bismuth per injection. The injections, roentgenographically, showed up clearly as a distinct blotch—though not as well and sharply defined as the salicylate. It was studied on nine different patients in a total of thirty-two different injections, the plates of three of which were worthless. Thirty-four plates in all were employed—with extremes of from four to ten plates and a median of six plates per injection. The deposit was totally absorbed in the following number of days: 6, 8, 8, 9, 10, 10, 10, 12, 13, 13, 14, 14, 15, 20, 22, 22, 22, 22, 23, 24, 24, 27; extremes of 6 and 27 and a median of 14 days in 22 of 29 different injections. In the remaining 7, it was not absorbed in 14, 20, 22, 24, 29, 29, 39 days, with extremes of 14 to 39 days and a median of 24 days.

COMMENT

The data gained from our roentgenographic study give us at once some new food for thought in regard to bismuth therapy. In general, the contention of the French writers that insoluble bismuth salts must be injected biweekly in order to have a gradual, even absorption of the metal is not borne out by our study. Levaditi himself has admitted that with some of the salts only infinitesimal amounts are absorbed at a time; and if the injections are given too frequently, is not one only building up excess metallic bismuth deposits that can do no especial good and that may do grave harm? Probably some of the salts should never be employed, and of those which we have studied only the best in matter of absorption should be given, not twice but once a week.

As a finely divided metallic bismuth is still unabsorbed after 143 and 150 days, one should not only hesitate, but one should probably never employ it because of danger of cumulative action. Certainly there would be grave danger in employing it twice a week, as is advised by various manufacturers and writers.

Therapeutically, our results with bismuth oleate have been disappointing, and we believe our roentgenographic study shows the reason. Bismuth oleate not only contains but 20 per cent. metallic bismuth, but it is also practically inert when deposited in the tissues. It is unfortunate that we have not had time to follow our patients further.

As we have already mentioned, we are hesitant in drawing conclusions as to the oxybenzoic acid salt of bismuth (Bismogenol), as only two injections were followed—though no appreciable absorption was noted in forty and forty-four days, respectively.

Bismuth salicylate is used widely in the treatment of syphilis and has been especially recommended and used in Germany. Herzog thinks it is the bismuth salt of choice. We personally have had excellent clinical results from its use, and believe that a good preparation of the salt is absorbed in time. However, since in only ten of forty-four injections was there complete absorption noted by the roentgen ray in a mean of forty-five days, one should be rather hesitant as to the too free use of this preparation, especially as deposits were noted even as late as 124 days after the injection. Certainly it is not to be recommended in biweekly doses, and is probably inferior to the potassium bismuth tartrate.

With the potassium bismuth tartrate our results were better, as absorption was noted in twenty-two of thirty injections in a mean of fourteen days. Even with this drug, however, in seven injections deposits were observed even as late as thirty-nine days. Probably cumulative action is not so likely to occur with this drug, especially if the patient is observed carefully and injections made only once a week intragluteally.

CONCLUSIONS

Study of the literature shows us that in the past bismuth has been the cause of many severe, chronic poisonings and even of fatalities. As various insoluble bismuth salts are now being widely used in intramuscular injections for the treatment of syphilis, it is well that we choose those salts giving the best therapeutic action with the least toxic disturbance.

The roentgen ray allows us to follow the rate of absorption of bismuth salts even as well as the salts of mercury.

A study of cases in which patients received injections with certain of the bismuth salts deep into the lumbar muscles gives us the following data: (*a*) Finely divided metallic bismuth was unabsorbed in extremes of forty-four to 150 days and a median of 143 days. No case of absorption was observed. (*b*) Bismuth oleate was unabsorbed in extremes of twelve to sixty-eight days and a median of twenty-six days. No case of absorption was observed. (*c*) In two observations, no absorption of oxybenzoic acid compound of bismuth was noted after forty and forty-four days, respectively. (*d*) In only 10 of 44 injections of bismuth salicylate was complete absorption noted in a medium of plus 45 days, while the injections were still unabsorbed in 34 instances with extremes of 14 and 124 days and a median of 30 days. (*e*) In 22 of 29 injections of potassium bismuth tartrate total absorption was noted in a median of 14 days and extremes of 6 to 27 days, while it was unabsorbed in 7 injections in extremes of 14 to 39 days and a median of 24 days.

These findings indicate that injections of metallic bismuth are dangerous and if persisted in will lead to cumulative absorption and possibly even to fatal results. The same is probably true although to a lesser extent of bismuth oleate. Bismuth salicylate likewise is not above this objection, and its use should be replaced by one of the more soluble bismuth salts—perhaps the potassium bismuth tartrate preparations. These salts, especially if injected intragluteally once a week, are probably not so likely to give rise to cumulative action. However, the patient should be observed closely, as even this salt is not above criticism so far as its absorption is concerned.

The contention that insoluble bismuth salts must be injected twice weekly is open to question, as only a small amount of the salt will be absorbed at the most. Moreover, too frequent deposits may lead to cumulative action, toxic symptoms and even the death of the patient.

DISCUSSION

Dr. J. Frank Schamberg, Philadelphia: I think Dr. Cole has presented to us some valuable data that are not only of scientific importance, but also of considerable practical weight. We have for several years been employing bismuth extensively in our clinic and have given probably several thousand injections. We have given the bismuth salt once a week, and with the exception of a few cases of mild stomatitis we have not seen any unfavorable results.

I think that today bismuth is superior to mercury for the treatment of syphilis. In the animal experiments we have been able to destroy the spirochetes much more rapidly. They both act the same on the kidneys, but in my opinion the bismuth is less toxic and more therapeutic. I think it occupies a position between the organic arsenicals and mercury. It is our custom to use intravenous injections of organic arsenicals and at the same time injections of bismuth. We have seen no reason to depart from this method in view of the excellent clinical results and the absence of complicating features.

Dr. Augustus Ravogli, Cincinnati: I have used the preparation of the salts of bismuth with good results. I have used the insoluble salts of bismuth and have found that the patients suffer a great deal of pain on account of the intramuscular injection. I have returned to the use of the soluble salts of bismuth, bismuth tartrate of sodium and postassium, of which I give one injection every week, and I have obtained fine results. In cases of primary syphilis, I have had excellent results, but in the secondary stage, up to the time of the papular syphilid, I prefer the use of arsphenamin. In tertiary syphilis, the bismuth acts like magic. In one case of gumma in a woman who was brought to my office unable to walk following a course of weekly injections, the patient is now able to attend to her household duties. I have never seen a stomatitis from bismuth, and although I always examine the urine I have not yet seen a case of albuminuria from bismuth.

Dr. Richard L. Sutton, Kansas City: Three years ago I went over the literature on bismuth therapy thoroughly. Practically all of it was French, and nearly every preparation recommended was plainly "patent" or "proprietary," and the results did not impress me seriously. Recently, I had an opportunity to review the manuscript of a book on bismuth therapy which is soon to be published, and I was pleased to learn that the various preparations of the drug

are now emerging from the obscurity of so-called "secret remedies." I think that in bismuth we have a valuable agent, particularly in the arsenic-fast and mercury-fast cases.

Dr. John H. Stokes, Philadelphia: I would like to ask Dr. Cole whether, in his roentgen-ray studies, he has seen any evidence of delayed or gradually diminished absorption following a series of injections of an insoluble salt. I have felt that clinically there is a gradual decrease in absorption toward the last of a series of insoluble injections, owing perhaps to fibrosis of the tissues into which the injection is made.

I should also like to ask whether Dr. Cole has seen any reports in the literature of explosive or violent reactions to insoluble bismuth salts such as were reported as a result of injections of mercurial (gray) oil.

Dr. Fred Wise, New York City: Is there undisputed evidence that the shadows thrown on the roentgenogram are actual gages of the absorption of mercury?

Dr. Thomas C. Gilchrist, Baltimore: It is interesting to us older men to have all these preparations running through the various arsenic compounds that we never saw in bismuth. It is confusing nowadays to teach a student the best method of treating syphilis. It still seems to be in the experimental stage. We used to advise marriage after a patient with syphilis had been treated with mercury and iodid, and many married without detrimental results. I think it is confusing to hear all the new things. We used to think that arsenic drove these organisms out of the body, and I suppose bismuth is doing it now.

The point is, are patients cured more rapidly by treatment with bismuth than they were before?

Dr. John A. Fordyce, New York City: Recent animal experiments have demonstrated that bismuth inhibits the growth and action of the spirochetes, but that they are not destroyed by this drug in therapeutic doses.

Dr. Grühzit (Parke, Davis & Company): I am thankful to Dr. Cole for this opportunity to make a few remarks. My experience has been entirely with work on animals in the laboratory, from the standpoint of spirochetal value as well as the value of the bismuth compound. In brief, I can say that my results have confirmed Dr. Cole's remarks. Bismuth is always absorbed slowly, but it is eliminated at a steady rate. For five months I have carried on a continuous examination of the urine and feces. The average elimination of the dog from the injection of a human dose was the same at the end as at the beginning of the series. Another dog receiving about three times the human dose, 100 mg., eliminated about twice the amount of the first dog; that is, about 0.4 mg. a day. The rate of elimination was surprisingly constant. It was not expected that bismuth would continue to be eliminated in that way. I find that about 80 per cent. of the bismuth is eliminated in the urine and only about 20 per cent. through the intestinal tract. The results may be slightly inaccurate because of the loss of urine and feces.

Another point is that if soluble, bismuth salt is injected into the muscle in a fan shape, not through the muscle tissue, but through the connective tissue binding the muscles together. That is true with all bismuth except the metallic bismuth, the French preparation. That cannot go through the lymphatic channels. In the injection of organic bismuth soluble or insoluble, except the metallic, it tends to spread in the fan shape, unless it is injected by force.

I have found another surprising thing, that when I kill animals—rabbits or dogs—when the roentgenogram does not show any shadow of bismuth on his-

tologic examination, there is plenty of bismuth. No matter whether you use the soluble or insoluble bismuth compound, it is the same. The bismuth remains there, not in the soluble form but in the insoluble form. I think I can explain this by the fact that when bismuth is mixed in an emulsion with an oil, the oil tends to become acid and precipitates the bismuth from soluble to insoluble, so that in the end it does not matter whether you use soluble or insoluble—it depends on whether the patient will take it or complains too much of the pain.

I have compared the effects of bismuth with those of mercury, and on the average I can say that in using mercury it is necessary to use four or five injections before the spirochetes disappear, while with bismuth only about two injections with the same interval are required. Inside of a week the spirochetes can be eliminated from the lesion, while it requires three or four injections of mercury, given twice a week. From that point of view bismuth is more effective. Just before I left Detroit, I had a lesion on a rabbit of which I was taking pictures from time to time, and the lesion under bismuth medication alone disappeared more rapidly than under mercury medication alone.

Dr. Harold N. Cole, Cleveland: I am glad to hear Dr. Schamberg say that he has been using bismuth just once a week, and I think that is one reason why he has had no toxic symptoms from it. I think we are more conservative here than on the other side of the Atlantic.

Replying to Dr. Stokes as to the explosive types of reaction, the only recent case of that type was one reported after sixteen injections. That case went almost to death. When we consider that bismuth therapy has just commenced, we shall probably have more of these in the future if we are not careful.

As to the gradual decrease and delay in absorption in the buttocks, we did not follow the bismuth from that standpoint, and at no time did we take pictures of the place where many injections had been made. We purposely took pictures where there was no chance for different injections to fuse together.

As to whether there is bismuth present after the roentgenogram shows that it apparently has disappeared, that question was answered by Dr. Grühzit. Injections have been made into animal muscles and have been followed by roentgenograms over a certain length of time, and then another picture has been taken and the bismuth found still to be present, and the area has been cut out and the amount of bismuth still present has been estimated. From 60 to 70 per cent have been found still present. It is true also that bismuth may still be present when it is not shown in the roentgenogram. This is only a comparative method of following it, and we do not say that if there is no shadow there is no bismuth present. We can say, however, that if the shadow is present after a certain length of time, some bismuth is present, and if injections were given too frequently they would cause trouble.

As to Dr. Grühzit's note regarding the gradual elimination of bismuth, we must be careful in saying that it will be a certain amount each day. Other investigators have not found this to be true. There have been marked discrepencies from time to time. With a drug like Neotrepol, even after five months there was evidence of bismuth in the urine.

Bismuth is a valuable drug in the treatment of syphilis. I think it has come to stay, but let us be conservative until we know just what it will do.

EPILATION IN MICE AS A BIOLOGIC STANDARD FOR DETERMINING ROENTGEN-RAY DOSAGE

PRELIMINARY COMMUNICATION *

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Methods of determining the dosage of roentgen rays are by no means solved problems. There are four general ways: the use of pastilles and radiometers, the arithmetical method, the electrical method and the biologic method. In America the pastilles have been discarded partly because of their poor quality, and partly because of the errors due to the personal equation in the interpretation of color changes, but chiefly because of the practical excellency of the arithmetical method. MacKee deserves the credit for the general adoption of this satisfactory scheme, based on the scientific observations of Shearer. Coolidge has made the criticism that various thicknesses of glass may result in variations of about 50 per cent. in the output from different tubes, but this criticism is largely offset by the fact that in the hand of numerous observers the epilation time in human beings is constant with many different tubes. That Coolidge's point has some practical value is borne out by the experience of one of us (H. H. H.), who found it necessary to increase the epilation time by 15 per cent. while working with an old tube which showed a heavy deposit in the walls. The use of ionization chambers is not nearly so satisfactory as some writers would have us believe. Satisfactory insulation is most difficult, and not always enduring. For practical use some of our best roentgenologists look on these machines as curses or sources of amusement. Biologic tests on the human skin would hardly appear justified in view of the serious results that may follow one erythema dose. In addition there are many inherent errors due to the personal equation. It is generally conceded by all roentgenologists who have had experience in the treatment of tinea tonsurans that the minimum epilating dose for the human scalp is an absolutely fixed and certain quantity, and hence should prove an ideal biologic check for dosage, were it only practical to use this method whenever desired. It occurred to one of us (H. H. H.) that it might be possible to utilize laboratory animals.

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* Read at the Fifty-Eighth Annual Meeting of the American Dermatological Association, Washington, D. C., May 4, 5 and 6, 1925.

The following problems were either evident before experimentation was started, or became evident as work progressed:

1. Mice were naturally chosen as the most available animals. The chief disadvantage is their liability to contagious diseases, such as mouse cholera. Twice has the importation of new mice resulted in serious loss of time and work.

2. The epilation time in mice is variously described as from four to six times that of man.

3. The constancy of response to an epilation dose could not be determined from the literature. Pfahler states that it varies 100 per cent.

4. The age, sex and size of the animal and the size of the area irradiated are unknown quantities.

5. The effect of previous radiation appears important. In a number of instances a temporary epilation was produced on an area about three-

TABLE 1.—*Results of Authors' Use of the Roentgen Ray*

Date of Irradiation	Dose in Units	Result
Oct. 28, 1924	4	20% in 6 weeks
Oct. 21, 1924	4⅓	35% in 6 weeks
Nov. 22, 1924	4⅓	35% in 4½ weeks
Nov. 22, 1924	4⅔	40% in 4½ weeks
Oct. 28, 1924	4⅔	50% in 6 weeks
Jan. 20, 1925	5	90% in 3 weeks
Dec. 13, 1925	5	Died 4 weeks, no epilation
Dec. 12, 1925	5⅓	10% in 5 weeks
Dec. 12, 1925	5⅓	50% in 4 weeks
Jan. 20, 1925	5⅓	25% in 3 weeks
Aug. 27, 1924	5½	50% in 3 weeks
Dec. 12, 1924	5⅔	10% in 5 weeks
Jan. 20, 1925	5⅔	60% in 3 weeks
Aug. 27, 1924	5¾	90% in 3 weeks
Dec. 13, 1924	6	100% in 3 weeks
Jan. 20, 1925	6	100% in 3 weeks
Aug. 27, 1924	6¼	100% in 3 weeks
Jan. 20, 1925	6¼	100% in 3 weeks

fourths inch square near the root of the tail. About three months later treatment of a small area between the shoulders resulted in a renewed epilation at the original site, long before the hair fell in the newly irradiated areas. This appears to us to be worthy of careful investigation. Certainly such an occurrence is unknown in man.

6. Numerous tubes, both old and new, must be tried.

7. The whole arithmetical system must be tested to determine its accuracy. Especially must the epilation at various distances and with various voltages be determined.

8. The inverse square of distance law as applied to filtered radiation must be determined.

9. Comparison with ionization chambers should be made.

10. The alleged effect of ultraviolet rays in preventing the usual sequelae of irradiation overdosage should be determined.

11. For radium the problems are naturally similar. The epilation time with various filters and at various distances must be determined.

Up to the present time only young male mice have been employed. All have been kept under identical conditions. The same transformer and Coolidge tube (No. 38,239) have been employed. A metal mouse cage with a hole in the back has been utilized for holding the animals during treatment. Up to the present time the standard technic of treatment has been: focal skin distance 9 inches, milliamperage 4, spark gap, 7½ inches (sharp points); no filter. The results of our experiments may be seen in the tables. We believe that the epilating time in young mice is constant, and that it is just six times that in man. Partial epilation in mice frequently occurs at intervals varying from four to six weeks; hence the correct standard is complete epilation occurring in three weeks. Twenty milligrams of radium in 5 mg. needles (Denver Radium Co.) were used. Manufacturers consider something over 97 per cent. of the rays to be gamma rays. In man the epilation time with this

TABLE 2.—*Results of Authors' Use of Radium*

Date of Radiation	Time	Result
Feb. 9, 1925	15 min.	100% in 4 weeks; previously irradiated
Feb. 9, 1925	20 min.	100% in 5 weeks; not previously irradiated
Feb. 9, 1925	25 min.	80% in 5 weeks; not previously irradiated
Dec. 2, 1924	25 min.	80% in 3 weeks; not previously irradiated
Feb. 9, 1925	30 min.	100% in 3 weeks; not previously irradiated
Dec. 4, 1924	35 min.	100% in 3½ weeks; not previously irradiated
Dec. 4, 1924	40 min.	100% in 4 weeks; not previously irradiated
Dec. 14, 1924	40 min.	100% in 4 weeks; not previously irradiated
Aug. 29, 1925	45 min.	100% in 3 weeks; not previously irradiated
Aug. 29, 1924	60 min.	100% in 3 weeks; not previously irradiated
Aug. 29, 1924	90 min.	100% in 3 weeks; not previously irradiated

radium is between seventeen and nineteen minutes. In the mouse it appears to be forty-five minutes. A certain number of our radium experiments are apparently invalidated by the fact that these mice were previously used for roentgen-ray experimentation. We are unable to state why the epilation time in mice with roentgen rays is six times that of man, while with radium it is but twice the time. It is probable that experimentation with high voltage rays will afford a key to this problem.

DISCUSSION

DR. GEORGE MILLER MACKEE, New York: The establishment of a biologic standard by which one may control practical technic and test a new tube constitutes a valuable addition to our methods and adds to safety and accuracy of technic

DR. RICHARD L. SUTTON, Kansas City: Experimental study of this character enables us to do accurate and scientific work with the roentgen ray in actual practice. I feel that many of the manufacturers have not played fair. They will sell a powerful machine to any one, no matter how ignorant or untrained he may be. The result is a long train of damage suits which fall alike on the unjust and the just.

DR. FRED WISE, New York: I should like to know whether the phenomenon Dr. Hazen described of the hair falling out at the tail and back of the neck is rare or frequent.

DR. FREDERICK D. WEIDMAN, Philadelphia: I should like to know about the duration of the epilation produced in this way. It would be useful in much of our animal experimentation to have an animal that could be permanently epilated. We usually have to clip the hair and then shave it, and by the time we are looking for lesions the hair has all grown in again. If this method will produce permanent epilation, it will still be of great advantage even after allowing for some abnormalities which would remain as the effect of the roentgen ray.

DR. HENRY H. HAZEN, Washington, D. C.: Replying to Dr. Weidman, the duration of the epilation depends on the dosage. With a small dosage it regrows as in man, but with a slightly higher dosage the epilation apparently is permanent.

Replying to Dr. Wise, it is a frequent occurrence to have the hair fall in that way.

INTRAVENOUS ADMINISTRATION OF SULPHARSPHENAMIN IN SYPHILIS*

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The manufacturers of sulpharsphenamin claim that it was placed on the market for use in patients who had veins so small as to preclude the use of the more effective arsenicals, arsphenamin and neo-arsphenamin. Because of its ready solubility in small quantities of water and its comparative freedom from irritating properties, sulpharsphenamin is particularly suited for intramuscular injection. In fact, some operators even prefer giving it by this route, urging that when given in this manner it is absorbed and eliminated more slowly, and consequently is more effective than when administered intravenously.

Stokes and Behn [1] report favorably on the use of sulpharsphenamin, particularly when given epifascially. They call attentior however, to its "distinctly increased tendency to cutaneous reactions as compared with the more familiar arsphenamines." Raiziss, Severac and Moetsch [2] have found that sulpharsphenamin, based on trypanocidal tests, was considerably inferior to arsphenamin and at most one-half as efficient as neo-arsphenamin.

During the past eight months, I have administered more than 400 doses of sulpharsphenamin intravenously to eighty-three patients. I selected those who had negative blood Wassermann tests when the treatment was begun. All, however, have been under my care for periods varying up to five years, and at one time or another they have shown positive Wassermann tests as well as active evidences of syphilis. They could all therefore now be classed as having arrested latent syphilis.

It is my custom, in cases of this type, to insist on the patients returning each year for a short intensive course of treatment, the usual regimen covering a period of twenty-eight days, during which time the patient is given daily intramuscular injections of one-sixth to one-fourth grain

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* Published with permission of the Surgeon General of the United States Public Health Service.

1. Stokes, J. H., and Behn, C. W.: Serologic and Clinical Results in Various Types of Syphilis, with Sulpharsphenamin Administered Intravenously, J. A. M. A. **83**:242 (July 26) 1924.

2. Raiziss, G. W.; Severac, M., and Moetsch, John: The Chemotherapy of Sulpharsphenamin, I. Toxicity and Trypanocidal Efficiency, J. A. M. A. **83**:1734 (Nov. 29) 1924.

(0.01 to 0.016 gm.) of mercury oxycyanate and eight injections of neo-arsphenamin, 0.6 gm. each, given biweekly into the vein.

In my experience, the objection most frequently voiced by the patients to the foregoing treatment has been with reference to the neo-arsphenamin. They almost all complained bitterly of the odor or taste of garlic or ether during and after the administration of the drug. In some, the unpleasant sensation was transitory while in others, with more sensitive stomachs, it was followed by nausea and vomiting. Some said that they experienced the taste constantly during the course of treatment, and a few insisted that it took months before they were entirely rid of the disagreeable sensation. The anticipation of being again subjected to a course of "that awful smelling stuff" was sufficient to deter many patients from pursuing their follow-up treatment, or at least to diminish their willingness to submit to it.

In cases of the type described above, it might be argued that, in view of the negative serology and the absence of clinical evidence, the virulence of the syphilitic infection is attenuated and consequently does not call as much for vigorous spirocheticidal treatment as it does for treatment designed to keep the infection under control. This line of reasoning prompted me to use sulpharsphenamin in these cases.

TECHNIC OF ADMINISTRATION

This was identical with that used for neo-arsphenamin. The drug was dissolved in 30 c.c. of distilled water and injected into the vein from a 30 c.c. all-glass Luer syringe. It was readily soluble and caused but slight irritation if a little of the solution leaked from the vein into the subcutaneous tissues. In no case was any tendency to thrombosis observed. The first dose was 0.4 gm., the subsequent ones were 0.6 gm., and the treatments were given every fourth day.

THERAPEUTIC ACTION

No critical study of the therapeutic activity could be made from this analysis, first, because clinical and serologic criteria were, for the most part, lacking, and second, because in all the cases mercury was used with the sulpharsphenamin, and it would be unfair to attribute any of the beneficial results noted to either one of the drugs. In general, however, it was evident that the results were fully as good as those observed with the older arsenicals. In this series are included twenty-four cases of neural syphilis. In all of these cases the results seemed superior to those usually observed after arsphenamin and neo-arsphenamin therapy. In two cases, severe lancinating pains were entirely relieved; in one case, a persistent diplopia completely cleared up, and in two cases in

which there was marked incoordination of the legs, there was remarkable improvement; whereas, in these five cases, previous treatment with neo-arsphenamin yielded indifferent results. It appears plausible that these observations are in keeping with the contention of Voegtlin [3] and others that sulpharsphenamin has a more selective action for neural structures than the older arsenicals.

REACTIONS

In no case was any kind of skin disturbance observed, either during or after treatment. This observation is particularly significant when compared with the reports on the subcutaneous method. In only three cases was there any gastro-intestinal disturbance. Two of these exhibited a transient nausea immediately after the injection, which disappeared in a very few minutes; in the third there was vomiting which lasted two hours. All three of these patients had previously had severe vomiting after arsphenamin and neo-arsphenamin. All of the patients in this series were quick to note the absence of any disagreeable odor or taste either during or after the injection, and were grateful for the change.

In the cases of tabes with lancinating pains, a distinct increase of the pains was practically constantly observed immediately after the treatments, the reaction being almost similar to that noted after intraspinal injections. This feature might be assumed to be due to the direct action of the sulpharsphenamin on the nerve roots. The pains usually continued for about thirty-six hours, and then subsided to a point where they were less severe than before the treatment was given.

SUMMARY AND CONCLUSIONS

1. In cases of syphilis which are Wassermann-negative and free from clinical symptoms, sulpharsphenamin seems quite as capable of controlling the disease as the older arsenicals.

2. From personal observation as well as the observations of others, it seems that sulpharsphenamin in neural syphilis is even more effective than arsphenamin or neo-arsphenamin.

3. Given intravenously, sulpharsphenamin did not produce dermatitis and caused practically no constitutional reactions.

4. On account of the absence of disagreeable reactions, patients submit more willingly to treatment with sulpharsphenamin, and consequently it is indicated in cases in which the maximum spirochetocidal effect of arsphenamin and neo-arsphenamin is not essential.

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3. Voegtlin, Smith, Dyer and Thompson: Public Health Reports, May, 1923, p. 1003.

ULTRAVIOLET LIGHT IN THE TREATMENT OF ROENTGEN-RAY TELANGIECTASES

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The use of ultraviolet light in the treatment of telangiectases produced by radiotherapy was discussed by Hazen [1] in 1922, but almost nothing else has appeared in the literature regarding the details of this method of treatment. It seems, therefore, of some value to report my own experiences in a case of chronic radiodermatitis in which I have had the patient under treatment and observation for the past four and one-half years.

REPORT OF CASE

A young woman, a school teacher, had a cervical adenitis, undoubtedly tuberculous, at the age of 13, with sinuses which persisted for five years. In 1913, 1914 and 1915, she had a long series, or rather several series, of roentgen-ray treatments, both unfiltered and filtered. The inflammation of the glands disappeared, and in 1920 she came under observation for her present condition. At this time she presented a large area of telangiectases and atrophy involving the whole upper half of the anterior chest, the anterior surface of the neck, and extending upward on either side of the neck in an inverted V-shape almost to the angle of the jaw. Just above the clavicle on either side there was considerable pigmentation, with scarring adherent to the underlying tissue, most marked on the right side, causing some restriction to the free movement of her neck. The condition of the skin on the front of her neck and on the sides was disfiguring enough to cause her to wear a high collar constantly.

Just before she came under observation at the clinic the use of ultraviolet light with pressure had been called to my attention. I started its use cautiously with a small round quartz applicator and moderate pressure, making application for only two minutes, and at first treating areas near the periphery on the chest. After three weeks these areas were definitely paler, and a longer time of application was used. The latter areas showed a definite disappearance of the blood vessels formerly so noticeable. The time of application varied from three to four and one-half minutes, and from three to six areas were treated at one sitting. She was treated at three to six week intervals during 1920, 1921 and 1922, but only a few treatments have been given during the last two years.

The reaction of the treated areas followed the usual course on normal skin. There was erythema and burning, with exudation of serum and lifting of the upper layer later, resulting in a flaccid bulla. This bulla ruptured, and the skin exfoliated, leaving a pink, smooth, sharply defined area. As this diffuse pink color gradually faded, it was noted that there were fewer large vessels than in the adjacent skin. The treated skin remained slightly glazed for several weeks.

The most improvement was noted on the sides of the neck, and she has been able to go about with almost no collar. The periphery of the area on the chest

1. Hazen, H. H.: The Ultraviolet Ray in the Treatment of Roentgen-Ray Telangiectasis, Am. J. Roentgenol. **9**:101, 1922.

showed marked improvement in the areas treated. Progress came to a standstill, however, and operative measures were suggested as the only means of relief. The patient acquiesced, and she has been referred for a plastic operation. This step has been hastened somewhat by the recurrence of enlarged glands just under the edge of the jaw, which are rather soft and probably tuberculous. There have also appeared, on either side just below the edge of the clavicle, two small, firm elevations, unchanged for the past year, but potentially degenerative. One of these elevations is in an area not treated, but the site of the other one has undoubtedly been treated.

COMMENT

From watching the treatment in this case certain observations have been made and certain lessons learned, which I believe may be of service to others with similar cases. In the first place, I wish to call attention to the effect of the ultraviolet light on the various characteristics of the affected areas:

1. The telangiectases have been obliterated very well near the periphery and in the smaller areas on the neck. These areas have remained practically clear from visible vessels for the past two years. There have been only two or three vessels in the neck which have been treated again in this time. The larger vessels have not been affected, and it is not advisable to increase the time or pressure enough to try to obliterate these.

2. The atrophy has remained the same. I believe there has been definite improvement in the texture of the skin in the neck, but in general there has been almost no change in the atrophic appearance.

3. The pigmented areas have not been affected. In fact, only a few of these areas have been treated—one or two of them repeatedly—but without any effect.

4. The scarring from the tuberculous process has likewise not been affected in the two or three areas treated. I have hesitated about treating these areas because of the infiltration and the fear of causing a slough.

In the second place, there are certain cautions to be registered in regard to this method of treatment:

1. Superficial ulceration, perhaps by reason of a low grade infection, can be produced by overdosage. This ulceration is slow to heal, in fact so slow that a suspicion of malignant change is aroused.

2. Treatment of too many areas or areas too near together are inadvisable at one time.

3. Cleaning the skin with alcohol or ether will increase the amount of reaction.

4. Itching may be increased, especially in cold weather, and one must guard against the trauma from scratching and the possible infection of these excoriations.

5. It is well to avoid areas of dense scarring and pigmentation because of the possibility of causing necrosis in the former and of stirring up melanotic changes in the latter.

As a result of this experience, I can recommend that a proper dosage, three and one-half to four and one-half minutes with pressure in the case of my lamp, or enough to produce flaccid vesiculation, should be used; that proper intervals both between areas treated and dates of treatment be observed, and that areas of telangiectases without marked atrophy and not too large can be benefited by ultraviolet light treatment. The seriousness of traumatizing a tissue already atrophic and degenerative by reason of an agent with a somewhat shorter wave length must be borne in mind, and the treatment should be undertaken with great caution, with a full knowledge of the abnormal tissue which is being treated, and with great care to prevent infection of the bullae and erosions produced by treatment.

Editorial

DERMATOLOGY TODAY

This is the season of the year when the dermatologists get together here and there over the country for their annual clinical meetings. These are a sort of dermatologic field days, and they give us perhaps our best indication of the actual state of the practice of dermatology.

One cannot attend these meetings without being impressed with the activity of dermatology now, the keenness of its practitioners, and their zest in its pursuit. One must also be impressed by the great development of dermatology during the first quarter of this century. Twenty-five years ago dermatologists for the most part were found in the largest cities, and not in all of them. Now first-class men are becoming widely distributed in the smaller cities, and we are getting expert service at the disposal of practically the entire country. This is a development that is not only a useful service to society, but highly salutary for the specialty. It is giving us a new element in dermatology which is detached, independent and stimulating.

The explanation for this sound growth of dermatology carries an interesting and instructive lesson. Dermatology in this country lately has grown from within. In the old days young men who hoped to become polished dermatologists went to Europe for their training. Now that is no longer the case. We have a few centers of dermatologic activity each of which is turning out a small but constant stream of trained men. These men receive an abundant clinical training. They become expert clinicians. In a few places also they are receiving sound training in the great fundamental sciences of dermatology, bacteriology and pathology. The chief criticism to be made of the experience our young men are getting as a whole is its lack of thoroughness in this training. There is need for strengthening our position in this respect. The ideal of training in dermatology should include, after a sound general training in medicine:

1. A practical working knowledge and skill in the pathologic histology and bacteriology of skin diseases.

2. A practical reading knowledge of French and German.

These things are easily acquired during the period of preparation, and they are so valuable in enlarging the field of the practitioner that they should not be overlooked at that time.

We are having a good deal of discussion now as to how specialists should be trained. In dermatology recent experience shows that the old practice is adequate, and probably the best one; the training in the specialty should be obtained from an apprenticeship under an expert or experts. Centers of good dermatologic training in this country are not due to any formal standardization, or university courses or to university affiliations. They are the work of expert individual leaders, sometimes training their disciples in independent hospitals and clinics, sometimes in university clinics, sometimes in private practice. Franklin said: "If you want to learn a trade, apprentice yourself to a master." All experience shows, from the example of old Socrates down, that that applies eminently to the highest vocations. W. A. P.

News and Comment

LOCAL DERMATOLOGICAL SOCIETIES

Manhattan Dermatological Society
David L. Satenstein, Sec., 116 West 58th St., New York City.
Max Scheer, Chairman, 616 Madison Ave., New York City.
Chicago Dermatological Society
Erwin P. Zeisler, Pres., 30 North Michigan Ave., Chicago.
New York Dermatological Society
Hans J. Schwartz, Pres., 50 East 53d St., New York City.
A. Schuyler Clark, Sec., 10 East 61st St., New York City.
New England Dermatological Society
Henry J. Perry, Pres., 19 Bay State Rd., Boston.
Wesley T. Lee, Sec., 220 Clarendon St., Boston.
New York Academy of Medicine, Section on Dermatology and Syphilis
Oscar L. Levin, Sec., 161 E. 79th St., New York City.
Fred Wise, Chairman, 40 E. 41st St., New York City.
Minnesota Dermatological Society
D. D. Turnacliff, Sec., Syndicate Bldg., Minneapolis.
St. Louis Dermatological Society
Norman Tobias, Sec., 516 Metropolitan Bldg., St. Louis.
Pittsburgh Dermatological Society
H. G. Wertheimer, Pres., Westinghouse Bldg., Pittsburgh.
Lester Hollander, Sec., Jenkins Arcade, Pittsburgh.
Detroit Dermatological Society
Howard J. Parkhurst, Pres., Toledo Medical Bldg., 312 Michigan St., Toledo, Ohio.
Philadelphia Dermatological Society
E. F. Corson, Pres., 1927 Spruce St., Philadelphia.
Patricia Hart-Drant, Sec., 2026 Locust St., Philadelphia.
Baltimore Section of Dermatology
Lloyd W. Ketron, Sec., 1107 St. Paul St., Baltimore.

FOREIGN DERMATOLOGICAL SOCIETIES

Italian Dermatological Society
Danish Dermatological Society.
La Societe Francaise de Dermatologie et de Syphiligraphie
Section on Dermatology, Royal Society of Medicine
British Association of Dermatology and Syphilis
Berlin Dermatological Society
Cologne Dermatological Society
German Dermatological Society in Czechoslovakia Republic
Vienna Dermatological Society
Munich Dermatological Society

APPOINTMENT OF DR. FOX

Announcement is made of the appointment of Dr. Howard Fox as Professor of Dermatology and Syphilology at New York University and as Visiting Dermatologist to Bellevue Hospital. It is of significant interest that this chair is one of syphilology and dermatology. The appointment is, of course, a well merited one. Dr. Fox will bring distinction to the institution.

CORRECTION

Dr. Charles J. White calls attention to an error in the prescription for crude coal tar incorporated in his discussion of this subject before the American Dermatological Association, May 4, 1925, as reported in the ARCHIVES OF DERMATOLOGY AND SYPHILOLOGY, December, 1925, p. 896. The prescription should read: Crude coal tar, one-half drachm; zinc oxide, one-half drachm; petrolatum, one ounce. The author's comment is: "This is too good a prescription to be spoilt."

Abstracts from Current Literature

Ocular Manifestations in Serum Sickness. A. L. Brown, Am. J. Ophth. **8**:614 (Aug.) 1925.

This is a report of ophthalmoscopic examinations in seventy-five patients who developed serum sickness after intravenous injections of diphtheria antitoxin. Ocular manifestations noted were moderate to severe hyperemia with or without serous exudate into the surrounding tissue causing papilledema in 20 per cent of the cases. Vascular dilatation was observed within fifteen minutes of an injection. In fifteen of the cases urticarial reactions were present, and in these cases it was observed that the ocular manifestations varied directly in intensity with the urticaria, and developed with the onset of the urticaria in the same manner as previously noted, subsiding with a subsidence of the urticaria. Epinephrin had a temporary inhibitory effect on the ocular reactions in these cases.

Foerster, Milwaukee.

The Wassermann Reaction and the Patient: Result of Routine Treatment of Eleven Hundred and Seventy Cases of Syphilis. F. C. Knowles, J. B. Ludy and H. B. Decker, J. A. M. A. **85**:1267 (Oct. 24) 1925.

The authors have reviewed their experience for a two year period in a large clinic for patients with syphilis. Of 1,170 patients admitted, 380 completed the first course, and 116 two courses. Treatment lapsed in 474 patients during the course of neo-arsphenamin, and in 316 during the course of mercuric salicylate. The large number of deserters is partly accounted for by the high percentage of negroes and sailors who attended the clinic. There were no serious reactions; although two cases of dermatitis and twenty of jaundice occurred.

This report contains a great deal of statistical data, too detailed for abstracting, but it shows that only one third of the patients completed the first course and only one tenth two courses of neo-arsphenamin and mercury. The authors are concerned about the amount of delinquency among their patients.

Effect of Treatment on Spinal Fluid in Cerebrospinal Syphilis: Critical Analysis of One Thousand Spinal Fluid Examinations. U. J. Wile and H. L. Keim, J. A. M. A. **85**:1269 (Oct. 24) 1925.

In their studies on syphilis, the authors have been impressed with the finding in many patients of a clinical cure which was not accompanied by serologic improvement. In the present study they have analyzed 1,000 spinal fluids obtained in 148 cases of neurosyphilis, from the standpoint of the parallelism of clinical and serologic progress. These patients have been treated for more or less prolonged periods with modern methods, including intraspinal therapy.

They found that in early cerebrospinal syphilis clinical and serologic improvement went hand in hand. In nineteen cases of this group, fourteen patients showed a complete return of the cerebrospinal fluid to normal.

In late diffuse cerebrospinal syphilis this tendency toward normality in the fluid is less noticeable.

In tabes and paresis, the parallelism between clinical and serologic improvement was practically absent. In none of the cases of paresis did the spinal fluid return to normality, although clinical improvement occurred in sixteen of forty-nine cases.

In tabes the spinal fluid changes were neither indicative of clinical improvement or the reverse.

The findings show that the lymphocytes are the most easily influenced by treatment; globulin, colloidal gold curve and Wassermann reaction following in the order named.

CLINICAL MANAGEMENT AND RESPONSE OF TABETIC PATIENT. J. H. STOKES and L. W. SHAFFER, J. A. M. A. **85**:1271 (Oct. 24) 1925.

Stokes and Shaffer emphasize the importance of an early diagnosis of tabes and call attention to the subjective symptoms which are significant. Among these lightning pains, cord bladder and paresthesia, all evidences of meningeal involvement, are the most common.

A determined effort should be made to reduce the spinal fluid to normal and keep it there, although this drive on the serology must not transcend the patient's ability to withstand the therapeutic assault.

They found that "stomach trouble," diplopia, vertigo, ptosis, girdle sensation and tinnitus respond to treatment in more than 50 per cent. of the cases, while failing vision, lightning pains, paresthesia, cord bladder, gastric crises, ataxia, deafness and optic atrophy show a therapeutic response diminishing in the order named. They found no improvement in ten cases of optic atrophy.

The article is replete with practical and valuable details of treatment.

SIGNIFICANCE OF NORMAL SPINAL FLUID IN CASES OF NEUROSYPHILIS. P. A. O'LEARY and M. O. NELSON, J. A. M. A. **85**:1276 (Oct. 24) 1925.

O'Leary and Nelson call attention to those cases of neurosyphilis with clinical evidences of the disease and negative serologic findings. With others, they have noted progressive changes in neurosyphilis unaccompanied by serologic evidence of the disease. In patients who still have clinical evidence of the disease, but whose spinal fluid has returned to normal as the result of treatment, they found that 70 per cent showed further clinical improvement when treatment was continued. In neurosyphilitic patients whose spinal fluid became normal without treatment, clinical improvement occurred in 45 per cent after treatment was instituted. A neurosyphilitic patient should not be discharged as cured after one negative spinal fluid report.

THE GASTRO-INTESTINAL SYMPTOMS OF NEUROSYPHILIS: DIFFERENTIAL DIAGNOSIS. M. FREMONT-SMITH and J. B. AYER, J. A. M. A. **85**:1282 (Oct. 24) 1925.

The mistakes that are likely to occur in differentiating gastric ulcer, gallbladder disease and other intra-abdominal disorders from tabes are discussed. In the group of fifty cases of tabes studied by Fremont-Smith and Ayer, twelve patients were operated on under mistaken diagnosis. The usual mistake is the unwarranted diagnosis of ulcer or gallstones instead of tabes. The intra-abdominal manifestations of locomotor ataxia range from unmistakable crises to moderate epigastric discomfort. In the differentiation the roentgen-ray is not wholly reliable, nor is a blood Wassermann test, which was positive in twenty-four cases and negative in sixteen. However, all but one case showed

abnormality in the spinal fluid. The influence of antisyphilitic treatment on the tabetic symptoms is not uniform.

In all but three cases of this series, pupillary irregularities were noted. The knee reflexes were normal in fifteen patients. Pupillary irregularity is, therefore, of decided diagnostic importance.

ROENTGEN-RAY IN TREATMENT OF LOCAL INFLAMMATIONS, CELLULITIS, AND CARBUNCLES. F. M. HODGES, J. A. M. A. **85**:1292 (Oct. 24) 1925.

Hodges states that the roentgen ray acts almost specifically in carbuncles, twenty-four of his series of twenty-six cases responding promptly to this agent. The two unresponsive cases were early ones situated in the upper nuchal region.

In two early cases of erysipelas subsidence was prompt after a single exposure. Favorable results in chronic parotitis are also recorded.

The author relied mainly on the filtered roentgen ray.

IMMEDIATE METABOLIC DISTURBANCES FOLLOWING DEEP ROENTGEN-RAY THERAPY. II. PREVENTION AND TREATMENT OF UNTOWARD REACTIONS. H. P. DAUB, A. BOLLIGER and F. W. HARTMAN, J. A. M. A. **85**:1299 (Oct. 24) 1925.

In discussing the causation of radiation sickness, the authors confirm the finding of a rapidly developing alkalosis. In investigating this condition in laboratory animals (dogs), various agents for counteracting it were tested. They found calcium lactate and morphin of the greatest value, the latter invariably preventing the reaction in dogs and proving helpful in patients in whom irradiation had previously been followed by untoward effects.

LEUKOPLAKIA BUCCALIS: OBSERVATIONS BASED ON A STUDY OF FORTY CASES. H. FOX, J. A. M. A. **85**:1523 (Nov. 14) 1925.

Fox ranks syphilis first and tobacco second as predisposing causes of this condition. Other local irritants, such as jagged teeth, highly seasoned foods, etc., are also important predisposing causes.

Of the forty patients, only two were women. The average age of the patients was 48 years. Leukoplakia in the negro race is rare, the author having seen only four cases in twelve years despite unusual opportunities for observation of skin diseases in the colored race.

Prophylactic treatment is most important. All local sources of irritation must be removed. The author thinks it best in the milder cases to put prophylactic measures into effect and watch the result. When active treatment is required, radium and the cautery are of value. Recurrences, however, develop in a minority of cases with each of these agents.

MICHAEL, Houston, Texas.

REVIEW OF THEORIES OF MECHANISM OF ACTION OF RADIATION IN TREATMENT OF CANCER. K. W. STENSTROM, J. Cancer Res. **9**:190 (June) 1925.

The various accredited theories of the mechanism of action of radiation in cancer are reviewed and discussed, and the conclusion is reached that while radiation does not have a specific action on cancer, it does offer a specific mode of attacking the disease which cannot be reproduced exactly by any other means. The result of radiation of tumor tissue is probably due to a combination of local and systemic actions, including direct action on cell cytoplasm and nucleus, increased activity of surrounding tissues, disturbance of vascular supply,

action of organic products or by-products resulting from radiation, interference with colloidal systems, disturbance of osmosis through cell membranes, disturbance of salt metabolism and changes in the blood.

THE FURTHER STUDY OF A CANCER FAMILY. A. S. WARTHIN, J. Cancer Res. **9**:279 (June) 1925.

The author states that there is evidence available to support the inference that in man the susceptibility to cancer behaves as an inherited recessive character. The study covers an investigation of three generations from a cancerous great grandfather and shows, among 146 persons, a cancer incidence of 19.18 per cent. For the eighty-eight adult members, the incidence is 31.81 per cent. The average cancer age of the affected members was 37.9 years. Other outstanding features were a tendency to sudden development and rapid course of the adenomatous types and the susceptibility in the males to cancer of the gastrointestinal tract, and in the females to cancer of the generative organs.

NO IMMUNITY PRODUCED BY INOCULATING IRRADIATED TUMOR TISSUE. F. C. WOOD and R. E. PRIGOSEN, J. Cancer Res. **9**:287 (Sept.) 1925.

Six thousand experimental inoculations and more than 30,000 control inoculations with mouse and rat tumors failed to show that injections of irradiated tumor tissue produced either immunity or increased resistance to subsequent inoculation with live tumor tissue. The tumor tissue was exposed to about six erythema doses of roentgen rays. It was also shown that in animals in whom tumor grafts had been successfully planted subsequent irradiation failed to produce recession of growth of those tumors.

STUDIES IN BIOLOGICAL RESISTANCE TO MALIGNANT TUMORS. THE EFFECT OF ROENTGEN RAYS ON THE ANTIGENIC SPECIFICITY OF CERTAIN PROTEINS EXPOSED IN VITRO. C. Y. LING, J. Cancer Res. **9**:305 (Sept.) 1925.

The proteins represented by B. typhosus, horse serum and sheep erythrocytes did not lose their antigenic specificity when exposed in vitro to larger doses of unfiltered roentgen rays. It is assumed, therefore, that native protein is not appreciably affected by irradiation.

THE EFFECT OF A SINGLE INJECTION OF IRRADIATED SARCOMA CELLS UPON THE GROWTH OF ESTABLISHED HOMOLOGOUS TUMOR GRAFTS. J. C. SMALL, M. J. EVANS and E. B. KRUMBHAAR, J. Cancer Res. **9**:316 (Sept.) 1925.

The growth of established tumors of rat sarcoma was not affected by a single injection of homologous tumor cells devitalized by roentgen rays.

The same experiment by the same authors with multiple injections of irradiated sarcoma cells, three injections being given at weekly intervals, also failed to affect the tumor growth.

MEASUREMENTS OF ELECTRICAL CAPACITY OF BENIGN AND MALIGNANT TUMORS. CLINICAL SIGNIFICANCE. G. W. CRILE, J. Cancer Res. **9**:388 (Sept.) 1925.

Preliminary experiments on this subject showed that pathologic conditions were accompanied by consistent changes in electrical conductivity and in electrical capacity. The hope is expressed that such physical measurements will serve as clinical aids in the differential diagnosis between benign and malignant tumors.

LESSONS LEARNED FROM FAILURES IN THE ROENTGEN-RAY TREATMENT OF CUTANEOUS CANCER. HENRY HAZEN, J. Cancer Res. **9**:404 (Sept.) 1925.

A study of 244 unselected basal cell cancers showed 33 failures or recurrences within eighteen months of a first series of irradiations. In five cases the condition cleared up with further treatment; in several cases the patients discontinued treatment, and in twenty-two the treatment was a failure. Of the latter, six involved the cartilage of the ear or eyelids, four had been previously irradiated elsewhere, two occurred in operative scars and several involved the lips. It was observed that patients treated with 1½ skin units responded as favorably as those treated with 2½ skin units. Microscopic study of two ear lesions involving cartilage, one nodule removed from the center of a roentgen-ray scar and several lesions occurring in surgical scars showed an absence of either lymphocytic or fixed tissue cell infiltration.

The author concludes that roentgen rays do not kill cancer cells directly, in the dosage customarily used, but that they stimulate certain local defensive mechanisms, and that they may also possibly have a general immunologic action.

FOERSTER, Milwaukee.

FRENCH SOCIETY OF DERMATOLOGY AND SYPHILOLOGY, MEETING OF MAY 14, 1925. Presse méd. **33**:737 (June) 1925.

Vaccine Therapy in Soft Chancre.—Pautrier employed with success a specific filtrate of the bacillus of Ducrey obtained by Habadou-Sala, and in a few days he was able to cure, without injections, soft chancres and buboes which had already developed.

Cutaneous Cancer Cured by Radium Therapy.—Wallon presented a number of patients who had cancer of the skin and were cured by radium therapy with filtration; he allowed only the hard gamma rays to penetrate.

Degrais is partial to the utilization of the beta rays, and he thinks that it is useless to apply radium for from eight to fifteen days when one can obtain a cure in from twenty-four to forty-eight hours.

Belot thinks that most of the cases presented could have been cured with curettement and a single application of radiotherapy slightly penetrative, which requires only fifteen minutes.

Milian is of the opinion that thermocauterization gives excellent results and a good scar.

Vegetating Bromid.—Hudelo and Chabrum presented an infant of 28 months who one week after a bromid treatment was attacked by disseminated lesions characterized by a follicular pustule with an inflammatory areola in which the confluence formed large vegetating plaques.

Angiokeratomatous Type of Mibelli.—Hudelo, Caillaud and Chabrum presented a child, aged 13 years, who was attacked by lesions of the hands and feet of the angiokeratomatous type of Mibelli, a morbid entity which develops only on a soil impregnated by tuberculosis.

Lichen Spinulosus and Lichen Planus.—Jeanselme and Burnier presented a woman, aged 61, who had an attack of lichen spinulosus of the fingers, with a marked pruritus; a month later she developed lichen planus of the mouth and vulva. The authors say that although these lesions occur simultaneously, they are not identical; biopsy showed a lichen spinulosus.

Pityriasis Rubra Pilaris Familial and Hereditary.—Jeanselme and Burnier presented a child, aged 5 years, who had an attack of pityriasis rubra pilaris. This affection existed also in two brothers, the mother and three cousins.

Intradermal Vaccine Therapy in Sycosis.—Jean Meyer presented two patients who had a staphylococcic sycosis; in one this sycosis had been treated since 1921 by autogenous vaccine and roentgen-ray therapy without result. He had improved rapidly after a few large doses of intradermal vaccine in the cheeks.

Generalized Favus.—Louste and Leclere presented a young girl, aged 18, who had had favus on the scalp, hands and lower legs since she was 3 years old.

Lupus Pernio.—Louste, Caillaud, and Leclere presented a woman, aged 22, who had lupus pernio of the nose. There were old scars on the hands with deformity on the fingers. Cutaneous tuberculous reaction and inoculation into the guinea-pig were negative.

Post-Traumatic Alopecia Areata.—Milian presented a man who had a typical alopecia areata forty-eight hours after the injury to the scalp.

Small Epidemic of Pityriasis Rosea.—Chevalier reported a small epidemic of pityriasis rosea which he had had occasion to observe in a house of prostitution.

Subcutaneous Multiple Peripilar Fibroma of the Scalp and Neck.—Burnier and Rejsek observed a woman, aged 56, who since 6 years of age had had numerous solid subcutaneous granulations of the neck and scalp. Histologically, it was a case of small fibromas with peripilar predisposition.

FRENCH SOCIETY OF DERMATOLOGY AND SYPHILOLOGY, MEETING OF JUNE 9, 1925.
Presse méd. **33**:1050 (Aug. 5) 1925.

Pruritus with an Eruption of the Type of Lichen Ruber and of Pityriasis Rubra Pilaris.—Hudelo presented a man, aged 38, who, in January, 1922, had an attack of intense pruritus, first partial and then generalized, which was accompanied at the end of three months by an eruption of confluent papules nearly generalized with some lesions on the hands and feet. The blood showed a leukocytosis and 10 per cent. eosinophils.

Darier thought that this was a case of cutaneous leiomyoma.

Milian observed a similar case in a patient who later had an attack of mycosis fungoides.

Aseptic Deep Abscesses Following Injections of an Oily Suspension of Bismuth.—Lortat-Jacob and Roberti reported three cases of tumefaction in the buttock following some oily injections of bismuth. Incision gave issue to an oily liquid containing bismuth (cultures negative).

Flandin and Simon are inclined to hold the oily vehicle responsible for this rather than the bismuth.

Cutaneous Circulation in Alopecia Areata and Vitiligo.—Levy-Franckel, Guillaume and Juster have examined by the capillariscope a certain number of alopecia areata plaques and spots of vitiligo. They have observed edema and a diminution or disappearance of capillaries; often there exists a vaso-constriction of the capillaries of the extremities of the fingers in patients with vitiligo. The aspect is, in general, the same in all the depigmented zones; on the hyperpigmented zones, on the contrary, the capillaries are extremely developed. After the application of the high frequency current (one-half minute), the capillaries become visible, but are always more abundant on the pigmented zones.

McCAFFERTY, New York.

A Peculiar Variety of Achromic Lichen Planus. G. Verrotti, Gior. ital. di dermat. e sifil. **66**:1173 (Aug.) 1925.

The author reports five cases of this rare malady. The condition is symmetrical and limited to the uncovered parts. There are usually two or more patches on the face and hands, composed of milliary, whitish, achromic papules covered with minute scales. These papules coalesce to form larger ones which in the course of time clear up in the center and spread peripherally. There is no atrophy or scar formation, and after recovery the skin appears normal.

Cutaneous Perithelioma. G. Berti, Gior. ital. di dermat. e sifil. **66**:1186 (Aug.) 1925.

The patient was an Italian woman, aged 60, who complained of numerous small, nodular tumors of the abdomen and thorax. They were removed surgically. Pathologically, there was a closely packed infiltration of endothelioid cells in the reticular layer of the corium, in the midst of which numerous lymphatic cavities and channels could be seen. The author gives a detailed account of the pathologic findings and differential diagnosis.

A Case of Syphilis of the Bladder. Tito Lucri, Gior. ital. di dermat. e sifil. **66**:1255 (Aug.) 1925.

A woman, aged 34, suffered from cystitis. Cystoscopic examination revealed the presence of a diffuse erythema of the posterior wall of the bladder and numerous lenticular dark red spots below the orifice of the left urether. The Wassermann test was four plus. There were no other symptoms of syphilis. The patient recovered rapidly under antisyphilitic treatment.

Pardo-Castello, Havana.

Stabile Recurrent Scarlet Fever-Like Eruption in a Case of Tuberculosis of the Lungs. A. Schock, Dermat. Wchnschr. **80**:197 (Feb. 7) 1925.

In a case of tuberculosis of the lungs the author reports a perifollicular, reddish, macular eruption of universal distribution, including the soles and palms. The eruption became more evident by its deeper color and was accompanied by itching after each severe paroxysm of coughing. True scarlet fever eruption and foreign protein rashes were ruled out by observation and the use of the protein skin tests. The author takes occasion at this point to state that in his hands these skin tests are of doubtful value. Biopsy of the involved skin showed only moderate perivascular infiltrate made up of eosinophils, lymphocytes, plasma cells and some mast cells. No tuberculosis bacilli could be demonstrated, and animal inoculation was not done. The name scarletiniform tuberculid is given to this rash.

The Etiology of Alopecia Areata. A. Buschke and B. Peiser, Dermat. Wchnschr. **80**:238 (Feb. 14 and 21) 1925.

The alopecia areata and other disturbances in growth (bones, etc.) obtained in earlier experiments by the authors by feeding thallium to rats lead them to draw parallel conclusions up to certain points, in alopecia areata in man, especially in reference to its etiology. Confirming recent reports in the literature and especially in the French journals, they cite clinical cases that have been under their observation to show that alopecia areata is due to central rather

than to peripheral disturbances. All cases can be referred to disturbances in the vegetative and endocrine systems. Diseased teeth (Jacquet), syphilis and other conditions only constitute irritants acting on these systems.

In a study of all the cases of alopecia areata seen at the Virchow Krankenhaus over a period of a year, in practically every case the authors could demonstrate abnormalities to a greater or lesser extent of a nervous, vegetative or internal secretory nature. Mental retardation, absence of the testicles, hyperorchismus, marked dermatographismus, defects in the growth of teeth, enlargement in the thyroid gland, vitiligo with vasomotor disturbances, abnormal sweat secretion, absence of the menses, disturbances in hypophysial function, etc., were some of the abnormalities found.

Syphilis does not assume such etiologic importance as once thought. The authors find no support for the contagious or parasitic theories. They resume their findings, saying that: alopecia areata is a definite clinical entity due to central disturbances probably of the vegetative-endocrine systems; the different external injuries noted in certain cases can only be regarded as contributory factors. Age, sex and family predisposition seem to exert a certain influence on the origin of alopecia areata. Although the possibility of an external infectious origin cannot be denied, its existence has not been proved.

VALUE OF THE SALICYLIC ACID AND THE THYMUS TREATMENT IN PSORIASIS. K. SCHREINER, Dermat. Wchnschr. **80**:281 (Feb. 21) 1925.

In ten cases injections of quinine and injections of emetin gave not a single successful result in the complete sense of the word. Following Sachs' advice, from 10 to 20 cc. of a 20 per cent solution of natrium salicylicum were injected intravenously every two to four days until from 20 to 30 Gm. were given. In twenty-three patients thus treated, one was clinically free from eruption fourteen days after the last injection, and two were somewhat improved. Using Brock's technic, thirty-two patients who had psoriasis were treated by irradiating the thymus, and the author noted a 50 per cent improvement to complete disappearance of the eruption in all cases. He considers that while the salicylic and emetine injections are of negative value, irradiation of the thymus is a valuable adjunct to the ordinary methods of treatment of psoriasis. (He makes no mention of any untoward or toxic symptoms arising as the result of irradiation of the thymus.)

INJURY TO THE KIDNEYS AND THE URINARY CANALS BY BISMUTH. W. ENGELHARDT, Dermat. Wchnschr. **80**:302 (Feb. 28 and March 7) 1925.

In general, the author's experimental results relative to the toxicity of bismuth for the genito-urinary tract and for the kidneys coincide with the results already published.

Twenty per cent of the patients treated with bismuth preparations showed pathologic changes in the urine, i. e., albuminuria, epitheliuria, cylindruria. One per cent showed a bacterial hematogenous nephritis. Fifteen per cent of all the patients treated were observed seventy-two days after the last injection and, with the exception of one patient showing epitheliuria for four weeks, the pathologic signs had entirely cleared up fourteen days after the end of the treatment. It could not be said that any definite amount of bismuth was necessary to cause a nephritis; however, shortening the interval between injections and increasing the individual dose bore a direct relationship to the appearance of stomatitis, gingivitis, etc. It is interesting to note that cysto-

scopic examination showed pathologic changes in the mucous membrane of the bladder before any subjective symptoms appeared. A great part of the cells found in the urine are no doubt due to a toxic cystitis.

LEUKODERMA ACQUISITUM CENTRIFUGUM (SUTTON). F. VON POOR, Dermat. Wchnschr. **80**:401 (March 14) 1925.

A woman, aged 33, was found to have about twenty pigmented papillomatous nevi distributed irregularly over the whole body. A large number of these nevi were surrounded by a band of white, depigmented and otherwise normal skin. Histologic study showed that this white zone is produced by a shifting of the pigment from it to the deeply pigmented nevi. The degree of depigmentation and the width of the depigmented zone vary directly with the intensity of the encircled nevus.

INVESTIGATION OF A STRAIN OF TUBERCLE BACILLUS RECOVERED FROM THE LUNG OF A PATIENT WITH BOECK'S SARCOID. KECK and MICHALIK, Dermat. Wchnschr. **80**:430 (March 21) 1925.

On the death of a patient showing a Boeck's sarcoid and dying of inflammation of the lungs (Michalik: Dermat. Wchnschr., No. 16, 1924), the fragments of the lung from which a strain of tubercle bacillus of either the human or bovine type was cultured, were inoculated into successive groups of guinea-pigs and rabbits. This strain was found to be pathologic for both types of animals, as is the human strain. The acid-fast bacilli recovered in stained smears from the internal organs of the inoculated animals were longer from those originally recovered from the lungs of the patient, and closely resembled the human type. Although the bacillus recovered from the patient's lungs was of a high toxicity for the experimental animals, pieces of the skin lesions (Boeck's sarcoid) when inoculated gave negative results. This helps to strengthen the ever growing theory that Boeck's sarcoid and the tuberculids in general are produced by a few bacilli of a high toxicity. It also accounts for the fact that so many of the histologic searches for a bacillus in skin sections have been negative and for negative results with animal inoculations with pieces of the skin lesions.

McCARTHY, Washington, D. C.

FINAL RESULTS IN ROENTGEN-RAY TREATMENT OF TUBERCULOUS LYMPHOMAS. GÖSTA RUNSTRÖM, Acta radiol. **3**:486 (Dec.) 1924.

The author employs from four to six series of single doses of one-fifth to one-third erythema dose, using the 15 inch spark gap, 12 inch target-skin distance, and 4 mm. of aluminum or 0.5 mm. of copper filter.

OPTICAL CHARACTERS OF LUPUS NODULES AND BEARING ON THE FINSEN TREATMENT. H. HAXTHAUSEN, Acta radiol. **3**:494 (Dec.) 1924.

Lupus tissue is especially transparent to the therapeutic light rays, it being shown that from two to six times the quantities of the desired rays penetrate 2 mm. of lupus tissue than can pass through the same thickness of normal tissue.

This selective action is considered the basis of the successful phototherapeutic treatment of lupus vulgaris.

INVESTIGATION INTO THE BIOLOGIC EFFECT OF FILTERED AND UNFILTERED ROENTGEN RAYS. L. ARNTZEN and C. KREBS, Acta radiol. **4**:5 (March) 1925.

These experiments were carried out with Victoria peas. An absolute stimulatory effect was proved with exceedingly small dosage. Single large exposures produced stronger biologic effects than the same dosage in divided form, and the biologic effects were found to vary directly with the ionization effect irrespective of the filtration employed.

RESULTS OF RADIOTHERAPY OF CUTANEOUS CANCER. WASSINK and WASSINK VAN RAAMSDONK, Acta radiol. **4**:146 (May) 1925.

The final results of 160 cases, observed between 1914 and 1922, in most of which the patient was treated with radium, indicated 81 per cent of success. For 116 cases not previously treated elsewhere, 89 per cent recoveries were reported. During the first eight years, twenty-five recurrences were observed, and all but one of these cases was cleared up with radium treatment.

FOERSTER, Milwaukee.

DERMATOLOGIC ABSTRACTS

THE JOURNAL OF THE AMERICAN MEDICAL ASSOCIATION

SODIUM THIOSULPHATE IN TREATMENT OF MERCURIAL STOMATITIS. G. A. M. HALL, China M. J. **39**:785 (Sept.) 1925.

Hall reports striking results from the use of sodium thiosulphate in four cases of severe mercurial stomatitis, and one case of tissue reaction due to the leaking of neo-arsphenamin from a vein. All the patients had an extreme degree of stomatitis. In none of the cases was there any gastro-intestinal disturbance, or any involvement of the kidneys. In two cases 0.45 gm. of chemically pure sodium thiosulphate, in 10 c.c. of water, was injected as the first dose, and no untoward effect was noted. A third patient, who was suffering considerably from syphilitic bone pain, and in whom it was desired to clear the condition rapidly in order that arsphenamin treatment might be started, was given one dose only of 0.6 gm. This was followed in about half an hour by a slight rigor, without, however, any further ill effects. The next day the mouth was so much improved that food could be taken with relish. Local treatment in all cases consisted of frequent washing out of the mouth with Dobell's solution. The patient with the arsphenamin in the subcutaneous tissue complained of great pain of a burning character, coming on very soon after injection, and after a few hours had considerable swelling and redness of the whole of the antecubital area. Ten patients received an injection of 10 c.c. of a solution containing 0.6 gm. of sodium thiosulphate.

Society Transactions

CHICAGO DERMATOLOGICAL SOCIETY

Regular Meeting, June 17, 1925

ERWIN P. ZEISLER, M.D., *Presiding*

PELLAGRA (?). Presented by DR. SENEAR and DR. WEBBER.

A man, aged 50, presented a dermatitis of one month's duration, which was confined to the dorsal surfaces of the hands. The neurologic examination was negative. The tongue showed smooth areas along the margin. He passed one stool a day. Examination of the lungs revealed pulmonary tuberculosis involving the right upper lobe. The patient said that a month before the eruption appeared he had lived on soup and "moonshine."

DISCUSSION

DR. MCEWEN: I believe this is a case of pellagra.

DR. ORMSBY: The limitation of the lesions to the dorsal surfaces of the hands is not the rule in pellagra. The dermatitis usually extends over the extensor surface of the wrists, then sweeps around and involves about two thirds of the flexor surface. This involvement of the wrist was a characteristic picture in many cases studied some years ago in the state institutions. In the patient presented, the mouth and cutaneous lesions are suggestive of pellagra. Pseudopellagra in alcoholic persons should be considered, as the patient is addicted to the use of alcohol, and this might prove the solution of the problem.

A CASE FOR DIAGNOSIS. Presented by DR. EBERT (by invitation).

A man, aged 36, first noticed an area of depigmentation at the external canthus of each eye about fourteen months before presentation. Similar areas gradually appeared on the face and neck. No change was noticed in the consistency of the skin, and there was no subjective sensation in these areas. In November, 1924, he noticed that the skin surrounding these areas was becoming markedly pigmented, and the disorder had spread to the shoulders and chest. In April, 1925, sclerodermatous changes were noted in the skin of the face. Erythema of the chest was observed two months before presentation and had persisted. During the summer of 1924, the skin of the hands became tender and itching blisters appeared from time to time. A tentative diagnosis of dermatitis herpetiformis was made at the industrial clinic at the Central Free Dispensary. He was given liquor potassii arsenitis (Fowler's solution), and the lesions cleared up. A short time before presentation there appeared large, tense, clear bullae on the dorsum of the right hand and on the nucha, with little itching.

The patient denied all venereal infection, but the Wassermann reaction had been positive on three examinations of the blood. The spinal fluid examination was negative. Beginning on May 26, the patient had received three injections of neo-arsphenamin at two day intervals, and had received two subsequent weekly injections of mercuric salicylate.

The face and neck were sclerodermatous. Irregular patches of depigmentation were surrounded by a deep brown hyperpigmented border in this area. The forehead was dark brown. There was a diffuse erythema of the chest and upper part of the arms. Scattered over this area were irregular patches, dull white to ivory, in which the skin was either atrophic or sclerodermatous. On the dorsa of the hands and on the nucha were a few pea to bean-sized, tense bullae, and several scars surrounded by a border of pigmentation.

DISCUSSION

DR. FOERSTER: I consider this an unusual case, and I believe that it should be investigated from a neurologic and endocrine standpoint. Syringomyelia should be considered, although the case at present is more like scleroderma. The occurrence of bullae and vesicles does not eliminate scleroderma, as they have been observed in sclerodermatous cases.

DR. ZEISLER: Is there any possibility of its being an atypical xeroderma pigmentosum? That occurs to me because the pigmentary changes are on the exposed portion of the body.

DR. ORMSBY: I think that Dr. Foerster has clearly stated the possibilities in the case. I believe the whole process is due to an endocrine disturbance, but I do not know which gland should be investigated. I can see how disturbance of the thyroid could produce all of the symptoms. I do not think it possible to name the disease, but I consider it a syndrome probably induced by endocrine disturbance.

PARAPSORIASIS. Presented by DR. ORMSBY.

A woman, aged 22, had a cutaneous disorder which had been present for ten years. She said that the eruption appeared rather suddenly, that no lesions had disappeared, and that there were no objective symptoms. The lesions were present on the thighs, the posterior surface of the trunk, the abdomen and arms, and occurred as superficial, round or irregular, sharply defined, pale or dull red, dime to dollar sized patches. Numerous brown, yellow and red puncta were seen. Some of the patches showed exaggeration of the normal lines of the skin, others slight scaling.

Histologically, there was a well-defined cellular infiltrate situated in the upper portion of the corium, composed of lymphocytes and connective tissue cells. There was also some infiltration around the blood vessels, coil and sebaceous glands. The epidermis showed slight hyperkeratosis and moderate hypertrophy of the rete.

DISCUSSION

DR. FOERSTER: I am impressed with the fact that some of the lesions are surrounded by blanched nonvascularized areas, and that they resemble small angiomas. The resemblance to Majocchi's disease is striking. As nearly as I can place the case, it belongs in the group of parapsoriasis.

DR. SENEAR: I think the sections are more nearly those of a distinct parapsoriasis than of any other condition.

DR. ORMSBY: When I first saw the patient his condition suggested other disorders to me, but parapsoriasis was one of the group. Study of the histologic sections decided the question.

LUPUS MILIARIS DISSEMINATUS. Presented by DR. LIEBERTHAL.

A man, aged 40, had never had a previous cutaneous disorder. His father was 67 years of age and well. His mother died at 60 of carcinoma of the stomach. Of his four children, one had died at the age of 3 years and another at the age of 3 months, cause unknown. The other two children were in good health. In 1920, the patient came under observation for pulmonary tuberculosis at the Michael Reese dispensary, and had since been seen at regular intervals. The pulmonary affection healed. The cutaneous affection had appeared about four months before presentation, with many pimples on the forehead. Gradually similar lesions developed on the cheeks. At no time did they cause any discomfort, nor did they show any changes. The eruption consisted of numerous papules on the forehead, cheeks and nasolabial furrows. They were bluish and yellowish-brown, pin point to pinhead in size, discrete and showed a central depression. There was no perceptible elevation. Slight pressure disclosed their softness, and the color did not change under the diascope. There were no secondary changes or coalescence. No other part of the integument and the mucous membrane showed any lesions. There was no glandular enlargement, and the blood Wassermann reaction was negative.

DISCUSSION

DR. ORMSBY: I believe that this is the first patient presented before the Society with this type of cutaneous tuberculosis, which was originally described by Tilbury Fox as disseminated follicular lupus. Later Crocker included it with his acne agminata, or acnitis. It is unquestionably a true tuberculous disorder, and the papules differ in appearance and career from those of ordinary lupus and acnitis. Wise and Satenstein recorded a group of this type under the name "lupus miliaris disseminatus faciei." It seemed certain that this patient exhibited this rare form of tuberculosis cutis.

DR. ZEISLER: How does this condition differ from miliary lupoid?

DR. SENEAR: I saw a patient, aged 70, who had several lesions scattered over the face, which resembled senile keratoses. On closer examination, disseminated lesions were found, pin point in size and exactly like those exhibited by this patient. The larger lesions showed the typical color of lupus vulgaris. We removed one of the small disseminated lesions of the type seen in this patient and found it distinctly tuberculous.

DR. FINNERUD: I understood that there is a difference between acnitis and disseminated follicular miliary lupus of Tilbury Fox. Last year I saw two cases in Vienna that presented exactly the same picture as that seen in this patient, and they were known there as "Akne telangiectodes of Kaposi." Does any one know definitely that the eruptions of Fox and Kaposi are identical.

DR. LIEBERTHAL: An interesting article on this subject, as well as on some other forms of cutaneous tuberculosis, by Kumer of Riehl's clinic in Vienna, appeared in the *Archiv*, volume 143. In the case which I have presented a microscopic diagnosis has not yet been possible, but sections will be presented at the next meeting of the Society.

ERYTHEMA MULTIFORME. Presented by DR. MITCHELL.

A man, aged 29, had had lesions of erythema multiforme limited to the mouth for five years. The attacks recurred every three months. This was the first time he had had cutaneous lesions, and when first seen, on June 8,

they were characteristic of erythema multiforme. The attacks last about three weeks. Before coming under observation, he had received twenty-three injections of neo-arsphenamin, under the mistaken diagnosis of syphilis. The lesions had begun to heal in the forty-eight hours before presentation.

DISCUSSION

DR. ORMSBY: I understood that this patient was presented because he had had a number of attacks of erythema multiforme limited to the mouth, which made the condition interesting. At present there are also some lesions on the arms. Dr. Oliver recently referred a patient to the Clinic who for ten years had had erythema multiforme limited to the mouth, and who had as yet had no lesions elsewhere. As the lesions in the mouth resemble those of pemphigus, the importance of their recognition is evident.

DR. MITCHELL: I presented the patient because most of the members saw the case presented by Dr. Butler last year, and also because it is interesting as arsphenamin has no effect on erythema multiforme. The man had received twenty-three injections, because the lesions in the mouth were mistaken for mucous patches.

LICHEN ATROPHICUS. Presented by DR. LIEBERTHAL.

A widow, aged 60, had never had any previous skin disease nor any severe illness. Her parents had died at an advanced age, and her three children in infancy. The present cutaneous disorder began about fifteen months before as white spots on her neck and wrists, which caused her no discomfort. About two months previously, itching spots had occurred on the right thigh. Examination revealed groups of roundish, pin-head to pea-sized, slightly depressed, white spots, some of which contained black follicular plugs, in the supraclavicular region on each side. Three similar lesions were seen over the upper part of the sternum, one group below the left scapula, and one on the nucha. On the volar surfaces of the wrists were numerous lesions with the same characteristics, but in none of these were there horny plugs. On the lateral aspect of the right thigh just beneath the lower gluteal margin there was a roundish erythematosquamous patch the size of a half dollar, which showed slight depigmentation in the periphery. About 4 inches (10.1 cm.) above this there was a round plaque of similar size consisting of slightly red papules, varying in size from that of a pinhead to that of a split pea, in close proximity to each other.

DISCUSSION

DR. ORMSBY: I agree with the diagnosis, and I believe the case belongs with the group reported at the St. Louis meeting of the American Medical Association in 1910. Later, with Dr. Montgomery, I recorded a similar group. In the beginning they were considered examples of white spot disease, but at present the belief is that there is no such entity. These cases belong to one of two groups, either lichen planus atrophicus or morphea guttata. Lesions of the type exhibited on the thigh of this patient have not been described in connection with this disorder.

DR. MITCHELL: Can we not add "hypertrophic," as the lesions on the leg are definitely hypertrophic?

DR. LIEBERTHAL: The lesions on the right thigh appear interesting and important. I shall try to secure permission to exercise tissue from these for microscopic study, although the patient thus far has refused to have this done.

ONYCHOSCHIZIA: KOILONYCHIA. Presented by DR. ORMSBY.

A man, aged 61, had had this disorder for twelve years. The first change noted was on the left ring finger. In the course of three years, all of the nails became involved, the disorder beginning in each instance on the distal end, or at the corner. At different times three of the nails had been shed. When presented, the nails were thin and depressed in the center, presenting transverse grooves on the surface. The distal third of some of the plates was undermined, elevated and separated from the nail bed.

Apparently there were two types of disease in this case: first, atrophy, which was producing the concavity on the surface of the nails, and which was more evident a year ago than at present; second, separation of the nail from its bed, the cause of which is unknown. It is not produced by any infectious disease, but may be of nervous origin. The patient had been treated with arsenic, with the idea that a change in the metabolism might improve the condition of the nails, and some improvement had occurred. To rule out ringworm, repeated microscopic examinations had been made and proved negative.

GRANULOSIS RUBRA NASI. Presented by DR. BEESON.

The patient, aged 20, had a condition that had appeared eight years before presentation. The patient said that the nose perspired even during the winter.

DISCUSSION

DR. LIEBERTHAL: I agree with the diagnosis. The case seems a little complicated because of numerous indentations in the nose.

DR. ZEISLER: It looks like a case of acne rosacea.

DR. ORMSBY: The diagnosis is probably correct. The small granular papules characteristic of this disorder are present, and there is also local hyperhidrosis. The cases are comparatively rare, but I presented a typical example before the Society in 1905. Two years previously, MacLeod gave an excellent summary of the subject. In the interval a few cases have been seen, and telangiectasia has not been present in any of the cases seen heretofore.

A CASE FOR DIAGNOSIS. Presented by DR. STILLIANS.

An infant, aged 4 months, presented a circinate, scarlike eruption over the lower part of the sternum and abdomen. There were diffuse pigmented areas over the forehead and temples. The baby was born after a normal full term, weighed 7 pounds (3.2 kg.), and was breast fed for the first ten days, then by artificial means, because of the death of the mother from a "blood clot." It was the second child, the first one having died of convulsions at the age of 6 months. The first child had had a similar rash over the body, and its legs were paralyzed. The father was living and well. The eruption began on the abdomen on the fifth day, and then spread to the face. At first it consisted of blotches of macular erythema, but when it spread to the face it was more like a purpura. There were no snuffles or ocular discharge.

The differential white count showed 84 per cent. lymphocytes, 8 per cent. large mononuclears, 8 per cent. neutrophils; the white blood count was 6,400.

DISCUSSION

DR. FOERSTER: The lesions on the abdomen terminated in scars and superficial atrophy, with follicular pitting. They were apparently of short duration and came on during the mother's illness, while she was nursing the child. The thought occurred to me that in a picture of this character, which was

not clear, one should think of dermatitis medicamentosa because of the possibility of the mother having received medication which was transferred to the child through the breast milk. The bromides came to mind, and the possibility if its being a bromid eruption. It might be well too look into the history along this line.

DR. STILLIANS: I have not thought of the question of medication, but I think probably an infection has caused the lesions on the abdomen.

CONGENITAL SYPHILIS. Presented by DR. STILLIANS.

This syphilitic infant had lesions involving the nails and the scalp. The child was underweight, not markedly marasmic, and showed several finger and toe nails which had been the site of an acute onychia, which was subsiding. These nails and one or two others were much narrower and more highly elevated in the center than normal. It was one of the few cases of "pinched" fingernails which had come under Dr. Stillians' observation. The scalp presented a large, partly bald area on the right parietal region and several small areas over the occiput in which the hair was very thin. Dr. Stillians thought the arrangement of the alopecia suggested syphilis.

PURPURA ERYTHEMA URTICARIAL (PURPURA URTICANS). Presented by DR. STILLIANS.

A laborer, aged 55, entered Cook County Hospital about June 1 with swollen ankles and a pale, macular eruption on the chest and extremities, which suggested a syphilitic rosacea. Some of the chest lesions were circinate, and following that red papules appeared on the body. He had no other symptoms, no sore throat or headache. There were no physical findings, and the urine was negative. He ran a low temperature. Since his admission to the hospital the lesions had become darker, suggesting a purpura, but they faded almost entirely on pressure. On the chest, back, arms and forearms a polycyclic erythematous eruption was present, with striking color, ranging from pink to purple. The legs were a uniform grayish-blue. The patient was very thin and had many bad teeth.

DISCUSSION

DR. ZEISLER: It is my impression that this condition was described by Osler under the name of purpura urticans. I saw this patient a week before, at which time there were definite urticarial lesions. I would suggest an infectious origin, cardiac or rheumatoid. So far as is known, this is the first attack.

DR. OLIVER: I would call it an urticarial erythema.

DR. ORMSBY: I do not think that the diagnosis of urticarial erythema would fit this case. I believe it is of toxic origin. Occasionally lesions of erythema multiforme and purpura coexist, and occasionally purpuric lesions have urticarial elements. In this interesting case there is a combination of these various types of lesions.

DR. STILLIANS: When the patient first entered the hospital the lesions were so pale that the intern thought of syphilitic roseola. I did not find much purpura, and I agree with Dr. Oliver that the case belongs in the erythema multiforme group.

NOTE.—About a week after the meeting the patient grew worse and was transferred to the medical service, where he died. A report on the necropsy findings will be submitted later.

ARGYRIA. Presented by DR. STILLIANS.

A nun, aged 60, had been troubled with a discoloration of the skin, especially of the face and hands, for thirteen years. There was some darkening of the body, but this was not as pronounced as on the exposed surfaces. There was no subjective symptom. Because of an ulcer of the stomach her physician had prescribed argyrol, 5 grains (0.32 gm.), three times a day. She took this regularly for three months, and after that took about 5 grains a day for a year. She had a severe vomiting spell, and the physician who was called ordered the argyrol stopped. She had noticed that her skin was turning steel blue, but at that time it became much worse and had remained unchanged.

DISCUSSION

DR. ORMSBY: Was hexamethylenamin used in this case? Dr. Olson has reported great improvement in local argyria from the use of this drug. If localized argyria is so favorably influenced, generalized cases might be improved. During the past month a patient with the generalized type had been given sodium thiosulphate by intravenous injection. Some improvement had been noted, but this might have been due to less exposure to the sun's rays, as the patient was hospitalized during the treatment. In that instance silver nitrate had been taken by the patient over a period of five years for gastric ulcer.

DR. STILLIANS: I thought of trying sodium hyposulphite in the case, although it would be exactly contrary to theory. It should fix the discoloration more firmly than ever, but as Dr. Fantus said, that the theory was all wrong, I shall give it a trial. I am interested in Dr. Ormby's success in the other case and I am glad that he called my attention to Dr. Olson's paper.

LEPROSY. Presented by DR. SCHMIDT.

A Chinese, aged 41, entered the United States five years ago. At that time no lesions were present on the skin. Soon afterward a pimple appeared on the right arm, which grew slowly, but remained painless. Seven months before presentation, he noticed stiffness in the right hand, and that condition had grown worse. The patient also thought his arm had grown smaller.

Examination showed that the right hand and forearm measured 1 cm. less than the left. The muscles were atrophic, and tactile discrimination, pain and temperature sensations were absent in the right arm from the elbow down. The ulnar nerve felt like a tendon and was insensitive to pressure. There was a V-shaped, serpiginous, elevated, brownish-red, linear lesion on the upper right arm, 36 cm. in length, and averaging 0.5 cm. in width. The color persisted under diascopy. Nasal and nasopharyngeal smears revealed no lepra bacilli.

DISCUSSION

DR. STILLIANS: I saw the patient several weeks ago, and would be glad to observe the case under treatment. The condition of a patient at the Cook County Hospital some years ago with involvement of the right hand, forearm and arm cleared up entirely under treatment.

DR. ZEISLER: Sometimes we have as many as six or seven cases under observation at one time at the Cook County Hospital. These patients are kept for a time and then sent to Louisiana.

RECKLINGHAUSEN'S DISEASE. Presented by DR. MOHR for DR. OLIVER.

The case of a negress, aged 19 years and five months pregnant, was of interest because she was first presented before the Society about two years ago. At that time the diagnosis was multiple benign tumor-like new-growths of Schweniger and Buzzi, and this was concurred in by all the members present.

DISCUSSION

DR. SENEAR: When the girl was shown before she had only a few lesions. They were all elevated and of the type which was apparent at present. They could be reduced in hernia-like fashion, and suggested strongly the beginning of multiple benign tumor-like new-growths. Dr. Pusey agreed with that diagnosis and every one present concurred in it, except Dr. Waugh, who suggested that it might be a beginning Recklinghausen's disease. The development of the disease corroborated Dr. Waugh's diagnosis.

DR. ORMSBY: The case is interesting because Crocker years ago stated that the so-called multiple benign tumor-like new-growths were nothing more than lesions of Recklinghausen's disease.

DR. SENEAR: Someone else recently expressed the same idea, that the lesions are simply atypical Recklinghausen's disease.

PITTSBURGH DERMATOLOGICAL SOCIETY

Regular Meeting, Sept. 17, 1925

LESTER HOLLANDER, M.D., *President*

A CASE FOR DIAGNOSIS. Presented by DR. GUY and DR. JACOB.

A Spaniard, aged 38, presented an eruption of five years' duration, limited to the scalp and back. On the scalp there were numerous infiltrated plaques and two large plaques over the ears that were definitely verrucous. On the back there were a few scale covered, infiltrated papules, suggesting psoriasis or seborrheic dermatitis, and several other plaques with dry verrucous surfaces. Subjective sensations were lacking. Biopsy showed a condylomatous epidermis with edema and an infiltration limited to the papillary layer. The elements of the infiltration comprised small round cells and fibroblasts with a few plasma cells and multinucleated cells. Degeneration of the elements of the infiltration could be noted.

DISCUSSION

DR. BEINHAUER: The case presented many possibilities, syphilis and mycosis fungoides being most likely. The lesions on the scalp with circinate or serpiginous outlines and a tendency to nodular make-up are suggestive of syphilis. The lack of a premycotic stage and the improvement under antisyphilitic treatment favor the diagnosis of syphilis.

DR. WERTHEIMER: My first impression of this case was that the condition was psoriasis or syphilis. But when one considers the duration of the disease and the psoriasiform lesions with infiltration, mycosis fungoides must be considered.

DR. CRAWFORD: The lesions in this case suggest yaws. Lack of premycotic stage and response to arsphenamin rule out mycosis fungoides and strengthen the diagnosis of yaws.

DR. FISCUS: I believe the case is either yaws or tertiary syphilis.

DR. DOTY: A case similar to this which I saw in Detroit proved to be mycosis fungoides. It also showed temporary improvement under arsphenamin medication.

DR. GUY: I favor a diagnosis of mycosis fungoides on account of the microscopic picture. Against yaws is the fact that the patient has had the eruption for five years, but he has been in this country for fifteen years.

GRANULOMA INGUINALE. Presented by DR. GUY and DR. JACOB.

A colored man, aged 35, presented ulcerative lesions in the groin of five years' duration. At the base of the penis was a roughly triangular lesion measuring approximately 4 cm. on each side, and paralleling Poupart's ligament on the left side was one about 2 cm. wide and 10 cm. long. The surface of the latter was elevated and condylomatous. The center of the triangular lesion was slightly depressed, with a smooth grayish base, and the periphery presented the same appearance as the linear area. Both lesions were bathed in a mucopurulent secretion, and both lesions were on a rather indurated base. Subjective symptoms were lacking. Donovan's organism was demonstrated at the time of presentation. The condition had developed following incision of a bubo and had been slowly progressive. The patient improved remarkably in one week under daily administration of tartar emetic intravenously.

LYMPHANGIOMA CIRCUMSCRIPTUM. Presented by DR. GUY and DR. JACOB.

A girl, aged 7 years, presented a lesion at the base of the right side of the neck, extending up and outward from the sternoclavicular junction, measuring about 3 to 5 cm. The lesion comprised single and grouped, thick walled, rounded, opalescent vesicles. Biopsy revealed the characteristic endothelial lined cysts with a slight surrounding cell infiltration and new capillary formation.

ELEPHANTIASIS. Presented by DR. HOLLANDER.

A youth, aged 14, presented an enlargement of the right leg from the thigh to the toes. The leg did not pit on moderate pressure. The skin was harder than that of the opposite leg. The condition was progressive and had existed since birth. On the dorsum of the foot, involving the large toe and the next two toes, there was a patch of dermatitis showing a roughened verrucous surface, with deep lateral fissure formation. The blood Wassermann test was negative.

DISCUSSION

DR. CRAWFORD: I consider this a case of Milroy's disease or hereditary familial trophedema. On questioning the patient, I elicited the fact that a cousin had a similar condition. Contrary to Dr. Hollander, I felt that pitting is demonstrable by very firm pressure and is not in the skin but in the subcutaneous tissue. These cases, although usually unilateral, are not necessarily so, and the partial trophedema of the left leg is in keeping with the disease. I believe that there is a neurologic relationship in the condition.

DR. DOTY: The condition on the toes is probably caused by a fungus infection.

DR. HOLLANDER: The patient has not been thoroughly studied yet. The condition in the cousin's leg was described as "some lumps" which had been removed. The lesions on the foot are probably epidermophytosis as described by Pusey in this condition.

FOLLICULITIS DECALVANS. Presented by DR. BUSMAN.

A woman, aged 50, presented a generalized follicular, pustular condition of the scalp of two months' duration. The essential lesion was an inflammatory papule or pustule surrounding the hair shaft. There was crusting in the older lesions, and there were areas of almost total alopecia varying in size from 1 to 6 cm. in diameter. Several of these areas showed central scarring. The general character was unusual for a folliculitis decalvans, but the follicular pustular primary lesion, the alopecia and scarring suggested this diagnosis.

DISCUSSION

DR. CRAWFORD: I agree with the diagnosis. I do not feel that all the alopecia is due to the same process.

DR. BEINHAUER: I disagree with the diagnosis presented and offer the diagnosis of trichotillomania. The uneven patches of alopecia, the symptoms of crawling sensations and inside pressure on the roots of the hair, the deep excoriations, the lack of peripheral follicular involvement and the recent loss of hair from the eyebrows with no pathologic bases favor this diagnosis.

DR. JACOB: Since most of the areas of alopecia show no scarring and all lesions present are excoriated, I agree with the diagnosis suggested by Dr. Beinhauer.

DR. BUSMAN: I cannot convince myself that this is a case of folliculitis decalvans, but the patient is not neurotic, and the process is only of two months' duration. My second suggestion would be acne necrotica.

URTICARIA PIGMENTOSA. Presented by DR. WERTHEIMER.

A child, aged 2 years, since two months of age had presented an eruption characterized by yellowish-brown, split pea sized and slightly larger nodules on the trunk, extremities and neck. The eruption was not itchy.

ACNE URTICATA. Presented by DR. CRAWFORD.

A man, aged 31, for the past two years had had recurrent lesions which appeared suddenly as small, red, itching wheals and papules. Some of the lesions he excoriated with his nails in an endeavor to remove an imaginary body (eggs ?). They reached the size of a pea and became indolent, red crusted, infiltrated lesions, annoyingly itchy and persistent. They appeared on the scalp, face, neck, upper part of the back, buttocks and thighs. The skin showed some factitious urtication.

DISCUSSION

DR. BEINHAUER: The picture presented and the patient's attitude toward his condition lead me to offer the diagnosis of neurotic excoriations.

DR. FISCUS: Is there any history of morphin addiction?

DR. BUSMAN: The man is of a neurotic type, interested in his own condition and in being here. The lesions are in easily accessible parts and are typical neurotic excoriations.

DR. CRAWFORD: I regard acne urticata as distinct from neurotic excoriations, although the psychic element of the latter enters into this condition. However, the lesions appear anywhere, are always ushered in by an acute inflammatory, edematous, itchy papule which the patient excoriates and contaminates with staphylococci, which, as in acne varioliformis, probably accounts for the scarring. The patient is highly neurotic. I do not know of any morphin addiction.

PITYRIASIS CORPORIS. Presented by DR. WERTHEIMER.

A colored woman, aged 22, for two months presented a scaly eruption situated over the upper part of the back, deltoid region, arms, forearms and lower extremities. The patches varied in size from that of a penny to that of a silver half dollar, were depigmented and showed a fine branny scaling at the border. The blood Wassermann reaction and direct examination for fungi were negative.

DISCUSSION

DR. DOTY: I saw a number of cases in Detroit which appeared as pityriasis rosea and which later showed the same appearance as in this case.

DR. JACOB: I have seen several cases of pityriasis rosea recently which resembled this case very much.

DR. WERTHEIMER: My main reason for presenting this case was to become more familiar with the diagnosis of diseases in the negro. I do not know a better diagnosis than that offered. The condition responded to treatment with amoniated mercury.

FRED. M. JACOB, M.D., *Secretary.*

MANHATTAN DERMATOLOGICAL SOCIETY

October Meeting

DR. G. C. ANDREWS, *Chairman*

PURPURA HEMORRHAGICA. Presented by DR. WEISS.

A girl, aged 5, gave a negative family history. She had had no infection in childhood, except measles. There was no history of rheumatism. One year before presentation, she had had a mild attack of tonsillitis. Three weeks before, her mother noticed an eruption on the skin; since that time more of the patches had appeared. The patches varied in size from that of a pinhead to that of the palm. The patient also had coughed up some bloody sputum; otherwise she seemed well. She may have taken phenolphthalein, but there seemed to be no history of this.

DISCUSSION

DR. ROSEN: The presentor should have mentioned an important observation in this particular case, namely, that each lesion presented a secondary inflammatory swelling, as though it were thrombic, probably due to a streptococcus infection.

DR. ANDREWS: The fact that the child coughed up blood might point to the embolic origin of the eruption.

DR. LEVINE: The lesions show embolism in the skin. This condition is probably due to damage of the blood vessels themselves resulting in hemorrhage in the skin.

DR. SATENSTEIN: The fact which militates against these statements is the absence of any heart condition.

DR. WEISS: While all agree as to the diagnosis, the etiology still remains somewhat uncertain. I do not believe it was due to some toxic process. As to treatment, I would suggest the old reliable method of administering tincture of ferric muriate in doses of 5 drops to one half glass of water.

NEVUS (DEEPLY PIGMENTED). Presented by DR. OCHS.

A boy presented on the left side of the cheek, a pea-sized, deeply pigmented, flat but sharply outlined nevus of three years' duration. There was no infiltration.

DISCUSSION

DR. OCHS: When the child came to me for the first time, I was tempted to use solid carbon dioxide, but I hesitated. I used trichloracetic acid, with no results. Not long ago, I saw a case similar to this, and there was a discussion of the use of electric coagulation. I thought that this procedure might possibly be of interest in this case. I sent the patient to Dr. Wise for further advice, and then brought him here for further suggestions as to treatment.

DR. HOWARD FOX: I believe that this is the type of pigmented nevus that is potentially dangerous. The lesion is smooth and light blue. However, since the patient was only a young boy and did not need to shave, and since the lesion was not elevated very much, Dr. Fox thought it best to leave it alone. If the patient should want the lesion removed for cosmetic reasons, it could be done by the use of either electrocoagulation or carbon dioxide snow.

DR. SATENSTEIN: When the nevi are associated with hair, I do not hesitate to remove them, but in the case of smooth nevi like this one, I would advise not touching it.

DR. SATENSTEIN: A patient had a lesion on the buttock, which was electrocoagulated; the microscope did not reveal any malignancy, but a year later the patient had developed a large mass in the groin which was diagnosed as melanoma. The patient died of general metastasis in a short time. This lesion was similar to the one in question at this meeting. Dr. Wyeth, in operating, cut one-half inch outside the lesion itself, and he cut deep down into the fat.

DR. LEVIN: I have treated patients who had pigmented nevi, but all of the nevi were hairy. Even in those cases, however, I used endothermy deep down to the fatty tissue and quite a distance outside the margin of the lesion. However, none of the lesions were smooth.

DR. WEISS: I would advocate endocrine treatment. It must not be forgotten that there was a possible suprarenal disturbance combined with this condition, causing the pigmentation of the nevus by the presence of a hemolytic principle in the blood; hence the reluctance of attacking it surgically.

DR. MOUNT: This type of nevus should always be let alone.

DR. ANDREWS: There is a history in this case of a lesion of three years' duration which started as pin sized and which has grown to the present size, although it has practically been let alone. Might not letting it alone cause more trouble, since it is growing and since it is a potentially dangerous thing? Instead of surgical incision, radium in large doses could be used followed

by final removal of the lesion with a cutting current and the loop. In letting it alone, the physician has placed himself in a safe position. However, this is not entirely fair to the patient. Dr. Andrews favored eradication of this mole with heavy doses of radium applied to the lesion and the surrounding areas to the extent of about 1 inch (2.5 cm.). This would be sufficient to destroy the lesion completely. Later, after three or four weeks, it might be cut out with the loop. He had seen this done successfully in three or four cases. As a practical consideration, it is doubtful whether this lesion would not be tampered with, and the only way to prevent such tampering would be to eradicate it properly now.

Dr. Satenstein: More cases are safe when let alone than when an operation is performed. Many of the dermatologists could report cases of subsequent metastases when something had been done and nothing happening when something had not been done.

Dr. Ochs: A girl, aged 16, had a large nevus on the inner aspect of her thigh which was removed surgically last February. A large incision was made, and the nevus was cut out. Roentgen ray was applied followed by radium. The girl is now in the hospital with multiple melanosarcoma of the chest, arms, legs and back. The roentgenogram shows metastases in the spinal cord. She suffers from incontinence of urine and feces. In consultation with a well-known dermatologist, the suggestion was made that the resultant damage may possibly have been due to the forceps rather than to the actual cutting out. Dr. Ochs also cited the case of a woman who had a small pigmented nevus excised, and within something like three or four months she died.

Granuloma Inguinale. Presented by Dr. Oscar Levin.

H. B., a negress, married, applied at the Cornell Clinic for treatment of the condition of her genitals. The duration of the present raw condition was eighteen years, but the patient stated that prior to that a tumor of the vulva had been treated with radium (?). Examination revealed a raw, discharging, superficially ulcerated condition, involving the adjacent surfaces of the labiae majorae and minorae. The surfaces were bright red, shiny, smooth, moist and covered with a seropurulent discharge. The surrounding tissues of the external and internal genitaliae were swollen and contained irregular lobular tumors.

DISCUSSION

Dr. Fox: I think the diagnosis of granuloma is correct. It can be confirmed without great difficulty by proper search for the Donovan bodies.

Dr. Parounagian: Clinically I agree with the diagnosis. It is difficult to obtain Donovan bodies in a case of as long standing as this. In my opinion the best therapy would be injections of tartar emetic. The lesions as a rule heal under this treatment, and recurrences are common.

Dr. Oulmann: The lesions may possibly be of an epitheliomatous nature.

Dr. Levin: There is no evidence of epithelioma. The lesions as presented are characteristic in the absence of a deeply ulcerated lesion. The lesions are superficial, smooth and shiny. Adenopathy is usually absent.

A Case for Diagnosis. (Pityriasis Rubra Pilaris?) Presented by Dr. Ochs.

A man had had a dermatologic condition for the past three years. It had begun with the appearance of small, conical elevations, with hyperkeratoses,

primarily on the abdomen, but the condition had spread rapidly. The patient had received a number of arsenical treatments, both by mouth and by injection, and he now showed an arsenical pigmentation. When he was first seen in September, he had a generalized weeping condition. His face was fairly flooded with water, and the abdomen and penis were saturated with fluid. He was admitted to the Fordham Hospital where he now was. Dr. Ochs understood that he had been thoroughly examined at Mount Sinai Hospital where he had been for six months. He had also been to the Skin and Cancer Hospital, where a diagnosis had been made with which Dr. Ochs did not agree. He made the tentative diagnosis of pityriasis rubra pilaris.

DISCUSSION

DR. FOX: The man showed an extraordinary clinical picture. I do not believe it is a case of pityriasis rubra pilaris because the patient has a widespread dermatosis which does not involve the palms. I have never seen a case of this disease with such an extensive distribution in which the palms were not affected. I agree that the pigmentation is due to the arsenic which the patient has taken, but I do not understand the nature of the eruption itself. I would suggest a microscopic examination.

DR. G. H. FOX: I felt certain that this case is not one of lichen ruber or, as this disease is foolishly called, pityriasis rubra pilaris. In my experience, all cases of this disease present in the papular stage a typical appearance which is readily recognized. The lesions are conical, red and surmounted by a minute white scale. When the lesions coalesce, as they usually do, they form small scaly patches which look very much like psoriasis, but they do not occur in disks but often in long bands on the trunk and extremities, as was first pointed out by Hutchinson. When the disease has persisted for years and covered the entire body, it presents a different appearance, but the eruption is the same on all parts of the body. The skin now is thickened and rugous, but tumors are not present. In this case the tumors are somewhat suggestive of mycosis fungoides.

DR. ROSEN: I saw the patient at the hospital, and while some of the symptoms are still present, the clinical picture of the eruption when I first saw it was different. The patient when admitted to the hospital presented on his face a condition which ordinarily would have been called vesicular dermatitis or weeping eczema. On the trunk and lower extremities he presents an eruption which consists of marked brown pigmentation. The palms and soles are distinctly hyperkeratotic. At no time were there lesions in the mouth. Itching is pronounced, and the patient always has the desire to scratch. After the patient had been in the hospital for about three weeks, he presented, on the neck, small groups of vesicles which formed tumor-like masses, and at that time the possibility of mycosis fungoides suggested itself. A portion of the skin was removed on two different occasions, and the pathologists of the hospital reported inflammation. Dr. Highman reported that he thought the condition was vesicular lichen planus. The patient had received sodium arsenite on several occasions but when the urine was examined for arsenic, none was detected. He was also given sodium thiosulphate. The diagnosis made at the Skin and Cancer Hospital was Duhring's disease. On careful examination, it could be noticed that there was a tendency for the lesions to group themselves.

DR. LEVIN: The history of the patient showed that he had been treated for Duhring's disease. When I first saw the patient at Mount Sinai Hospital

there was an eczematoid appearance, but this gradually subsided, and the patient developed some tumor-like lesions which revealed nothing but chronic inflammation. When I saw the patient again at a later date, he showed hyperkeratotic follicular lesions, and the tumor formation was more pronounced. The various diagnoses suggested at the hospital were lichen planus, arsenical dermatitis, mycosis fungoides and pityriasis rubra pilaris. At this presentation Dr. Levin thought the patient showed a possible mycosis fungoides.

DR. OCHS: When I first saw the case, the patient had severe keratosis of the palms and soles. He also had the weeping condition. He said that he did not know of any case of either Duhring's disease or mycosis fungoides in which there was such a condition. For a while the keratotic patches had begun to disappear, but at present they were returning. The patient had been given potassium iodide internally, and salicylated oil externally which seemed to relieve him. He was now giving the patient tonics. Chronic inflammation was the only pathologic condition found.

DERMATITIS HERPETIFORMIS. (DUHRING'S DISEASE.) Presented by DR. WEISS.

L. L., from Dr. Weiss' service of the Stuyvesant Polyclinic, aged 35, Russian by birth, had a negative family history except that her mother suffered from frequent frights and died of meningitis. The patient had had no illnesses of childhood except measles. Later she was afflicted with bleeding hemorrhoids, rheumatoid pains and a leukorrheal discharge. The patient had never been pregnant. Her menses had always been regular; the last one was scant, however. She had recently developed an ankylosis of the right wrist. About five years before presentation the skin of the lower part of the abdomen suddenly became red and itchy. The same condition later appeared on the inner aspect of the thighs and outer aspect of the arms, whereupon the patient took a sweat bath which was followed the next morning by the appearance of oozing sores over the lower part of the abdomen. She went to the Skin and Cancer Hospital, and while there, the rash became generalized from the scalp to and including the toes and fingers. The patient remained in the Skin and Cancer Hospital for nine weeks and recovered, with a permanent condition of generalized macular pea-sized scarring with diminished pigmentation. Spells of improvement and aggravation of the eruption occurred in periods of six months to a year, and at present the patient was much improved. About one month ago she showed papular, vesicular, violaceous, crusted and scratched lesions on the limbs, neck and back. She also showed on the left palm and sole of the left foot a violaceous and tender edema, with a similar but milder condition of the right hand and foot. Her Wassermann test was negative; the blood count was normal; the urinanalysis was negative for albumin and sugar. The case was presented as one of Duhring's disease — a dermatitis herpetiformis followed by macular atrophy. Some of the lesions like those on the palms and soles resembled a phenolphthalein eruption. No test was made with phenolphthalein, but the patient had taken X-Lax frequently, which contains that drug.

DISCUSSION

DR. ROSEN: The patient had been at the Mount Sinai Hospital on different occasions. A photograph takene two years before presentation showed a most unusual type of dermatitis herpetiformis of the varioloid form. The patient presented a generalized pustular Duhring's disease. She had lesions in the

mouth and generalized grouped lesions on the trunk which were varioliform with a central depression. I believe the scars shown at this presentation are due to the involution of these pustular lesions.

PARAPSORIASIS (BROCQ TYPE). Presented by DR. SCHEER.

G. T., aged 23, a man, unmarried, a salesman, born in Hungary, presented himself at the Mount Sinai Clinic showing an eruption which had been present for four years and which appeared first on the day of landing in this country. The eruption appeared suddenly over a large area of the trunk and the extremities. There had bee no itching. The patient said that four months ago he received six alpine lamp treatments, with no benefit. He had never received injections of pilocarpin. From the clavicular and suprascapular regions, extending down over the thighs, both anterially and posteriorally, were numerous isolated and confluent plaques varying in size from that of a dime to that of the palm and in color from pale red to a distinct violaceous hue. These patches for the most part were sharply outlined and not scaly although a few of the small livid spots showed psoriasiform scaling. The eruption was also present on the inner sides of the arms, thigh, legs and dorsa of the feet, though much less pronounced than on the trunk. The general condition was good, and no lesions were present on the mucosae.

DISCUSSION

DR. PAROUNAGIAN: Dr. Scheer treated the case with injections of pilocarpine to note the therapeutic result.

DR. BECHET: I agree with the diagnosis; but there are two or three patches on the trunk, sharply defined, with a marked serpiginous outline and slight infiltration. These lesions warrant a careful watch for the possible development of mycosis fungoides. I would suggest a biopsy from one of these plaques.

DR. ROSEN: I believe the bright red lesions are unusual in parapsoriasis; as a rule, they are pale pink.

NEUROTIC EXCORIATIONS. Presented by DR. OCHS.

A man, aged 42, presented an extensive eruption on the scalp, arms, legs and buttocks. He said that three years before presentation, while in Toronto, a physician had injected some medicine into his blood. He believed the doctor injected living organisms into him in order to kill him and get the property to which the patient was entitled, and since that injection, he has been constantly "picking things out of his skin."

PAPULONECROTIC TUBERCULIDS. Presented by DR. LEVIN.

M. K., a man, married, aged 54, a tailor, complained of a persistent eruption of three years' duration, involving the forehead, extremities and trunk. Examination revealed about two dozen small pea to bean-sized, dark red and brownish red conical papules. Some of these were follicular and others nonfollicular. A few showed necrotic tops with finely adherent crusts, while the larger ones on the legs presented irregular ulcerations. General examination revealed only emphysema and chronic bronchitis. Roentgen-ray examination of the chest disclosed a general increase in the bronchial markings consistent with chronic bronchitis, but not definitely indicative of active disease. The Wassermann

test was doubtful. The blood examination showed the following: hemoglobin, 90 per cent; red blood cells, 5,120,000; white blood cells, 9,000; polymorphonuclear leukocytes, 40 per cent; lymphocytes, 58 per cent; eosinophils, 2 per cent. The piece of tissue removed for pathologic examination revealed a dense, round cell infiltration of lymphocytes and plasma cells around the pilosebaceous follicles. The granular layer was preserved and there was no edema, the structure corresponding to that form of granuloma occurring with papulonecrotic tuberculids.

DISCUSSION

DR. HOWARD FOX: I do not see any pitted scars characteristic of papulonecrotic tuberculids, and I do not see on what grounds such a diagnosis can be made in this case.

DR. LEVIN: Three weeks ago the patient showed the lesions on the arms. On palpation they felt infiltrated. The forehead and cheeks showed necrotic lesions. One of the lesions of the left arm was excised and the pathology was that of the diagnosis made. The examination was made by Dr. Frazier who had not even seen the case clinically.

DAVID L. SATENSTEIN, M.D., Secretary.

NEW YORK ACADEMY OF MEDICINE, SECTION ON DERMATOLOGY AND SYPHILIS

Regular Meeting, Oct. 6, 1925

FRED WISE, M.D., *Chairman*

PELLAGRA. Presented by DR. PAROUNAGIAN and DR. MASON.

J. B., aged 40, was admitted to the clinic, Sept. 22, 1925. He presented a marked pigmentation on the dorsum of both hands extending to the wrist, which had persisted since June, 1925. He had no diarrhea, mouth or mental symptoms, although he said that he had had diarrhea in July, and the dermatitis on the back of the hands was more marked at that time. He was a native of New York City, although five years before presentation he had resided in Virginia for two months.

While the case is not a typical example of pellagra, the pigmentation is suggestive of that disease.

DISCUSSION

DR. POLLITZER: I feel doubtful concerning the character of the case. The main feature, of course, is the pigmented condition of the hands, but that is not the only condition that the man presents. The line of pigmentation lacks even the characteristic oblique border, and other than the coloration there are no features of pellagra. Although it is possible from one foot to recognize Hercules, yet I would hesitate to diagnose pellagra from a pigmented dorsum manus.

DR. CANNON: I saw the patient at the hospital while the condition was in the acute stage, and at that time the diagnosis of pellagra was considered but was ruled out on account of the man's history, the marked local inflammatory reaction and the absence of constitutional symptoms. The patient was an indoor worker who, following prolonged exposure to the direct rays of the sun, had

an acute burn and secondary infection. His condition promptly cleared up under wet dressings of potassium permanganate, and was considered to be dermatitis due to sunburn.

DR. PAROUNAGIAN: The discoloration is the only sign now present, but the patient has a history of a scaling dermatitis on the dorsum of both hands since last June and diarrhea since July. I know of no other disease than pellagra that can produce such sharply outlined pigmentation on the dorsum of both hands and extend no further than the wrist. As to the fact that the man was born in New York City, that would not exclude the diagnosis. In a number of cases patients who have been born in New York and who have never left the city have developed pellagra. A young woman whom I saw in Bellevue Hospital on May 7, 1924, had dermatitis on the backs of the hands, diarrhea, lesions in the mouth and nervous exhaustion, from which condition she died one week later. She was born in New York and had never left it. She said that her sister-in-law had had similar sores in the mouth, an eruption on the hands and diarrhea. She had nursed her sister who had died of the same disease. I believe that there are more of these cases in and around New York which probably are not recognized. Recently I was called on to see at least five or six cases of pellagra at Bellevue Hospital.

LUPUS ERYTHEMATOSUS DISSEMINATUS WITH UNUSUAL DISTRIBUTION. Presented by DR. PAROUNAGIAN and DR. MASON.

Mr. L., aged 30, had had a skin affection for seven months. The affected areas were the face, scalp, neck, arms and back. The lesions were unilaterally arranged and running parallel to the spine. His Wassermann test was negative.

ARSPHENAMINE DERMATITIS. Presented by DR. PAROUNAGIAN and DR. MASON.

W. S., aged 27, was infected with syphilis nine months previously. He had consulted three private physicians. The first one treated the chancre locally, the second gave him twelve injections into the buttocks and the third ten intravenous injections. The general dermatitis manifested itself with marked exfoliation subsequently. He was admitted to the Bellevue Clinic on Aug. 27, 1925, the dermatitis having begun about two weeks previously. His Wassermann tests were negative on two occasions.

DISCUSSION

DR. ANDREWS: In a case of arsphenamine dermatitis of six weeks' duration, the patient had received eight doses of neo-arsphenamine. The eruption began on the face. Eight grams of sodium thiosulphate and local roentgen-ray treatment produced no results. Larger doses of sodium thiosulphate were then given intravenously, and the patient made rapid improvement. The sodium thiosulphate was then given by mouth, the improvement continuing for a week. After that, the patient neglected to take the thiosulphate and became rapidly worse, having a severe exfoliative dermatitis, with a temperature of 105 F and a pulse rate of 145, being comatose and having ulcers on both cornae. The thiosulphate was then again administered intravenously, 1 Gm. twice a day. This was followed by rapid improvement. A change from the dry thiosulphate prepared at the bedside to that already in solution was immediately followed by a slight relapse, the patient, however, improving readily on reverting to the former preparation.

DR. FRASER: In a similar case seen in 1924 sodium thiosulphate was administered without producing any improvement.

DR. ABRAMOWITZ: It has been decided definitely that the action of thiosulphate is to stimulate the kidneys to a greater output. In patients with arsenical dermatitis who have nephritis, other eliminative measures should be used and some calcium preparation, should be administered.

DR. POLLITZER: I do not see how one can expect much from the use of sodium thiosulphate in a case of dermatitis so pronounced. It destroys the arsenic as a poison and so stops its further action, but if the damage has already been done and the dermatitis developed, you are dealing with a condition that is established, and removing the original cause is not going to affect the established disease.

Referring to the cause of the production of the dermatitis, since I stopped giving weekly injections of the arsenical preparations, four, six, seven, or even eight injections as some of my colleagues employ, I have not seen a case of arsenical dermatitis in my practice. In my opinion, it is the injury caused by weekly insults over a long period of time that does the damage. During the last eight years, I have used both the old and the new arsphenamine.

DR. CANNON: I believe that most cases of arsenical dermatitis result from faulty elimination and improper treatment, as suggested by Dr. Pollitzer. I have never seen an arsphenamine dermatitis in any patient whom I have treated with the drug, but I have observed many cases in the clinics, hospitals and in consultation. I believe that when the proper technic and dosage at intervals are the rule, when the patient's elimination is carefully watched and when the drug is discontinued at the first indication of any itching or skin eruption, one can usually avoid an arsphenamine dermatitis.

A few years ago I treated several patients with the roentgen ray without noticing any change in the eruption. As for sodium thiosulphate used internally, I believe that it is sometimes difficult to tell whether it is beneficial or not. I have used that drug intravenously in a series of cases, while in others I have given forced fluids, colon irrigations and saline cathartics, with about the same results in each series.

As Dr. Pollitzer has pointed out, when a patient has fully developed an arsphenamin dermatitis, one cannot expect a rapid improvement with the use of sodium thiosulphate. In severe cases I think that bleeding of 200 cc. of blood every few days, as practiced by European physicians, often proves beneficial.

DR. WOLF: Only adverse reports have been heard. I should like to report the case of a patient whom I treated this summer. The patient, a woman from Texas, treated with arsphenamine intravenously after the eighth injection developed a severe arsenical dermatitis. The physician in charge was much perturbed. I then gave the patient sodium thiosulphate intravenously, and to my great surprise the dermatitis cleared up rapidly. Whether to attribute this improvement to the sodium thiosulphate or to something else, I cannot say, but I do believe that it was useful in this particular condition.

DR. GOODMAN: I have had a varied experience with arsphenamine dermatitis, and have found sodium thiosulphate efficacious. At an earlier meeting of the Section, I said that I have used prophylactic doses of this drug alternately with injections of the arsphenamine preparation. I hesitate to introduce several instances, but I feel that they are illustrative. This past summer I saw two

cases of arsphenamine dermatitis, one in the patient of a colleague. The patient had received fourteen injections biweekly, the last when he reported to his physician with the skin of the palms exfoliated. This patient was seriously ill. Sodium thiosulphate was administered, and the attending physician gave the drug intravenously through error. The patient recovered. In the second case, the patient received the same brand of drug as the first patient, and developed dermatitis, elevation in temperature, pruritus and other attending symptoms after two injections given at five-day intervals.

I do not approve of the concomitant use of an arsenical and a mercurial; but I believe that for the patient with syphilis one of these heavy metals is enough at one time. In the case shown, it might have been the mercury which caused the eruption. The German literature shows many such instances.

DR. ANDREWS: I question whether this is purely an arsenical dermatitis caused by excretion of arsenic by the skin, since the severity of the eruption seemed out of all proportion to the amount of arsenic taken. Is it not, rather, a protein intoxication due to the catalytic action of the arsenic? I consider that the value of sodium thiosulphate is rather definitely shown in this case.

LUPUS ERYTHEMATOSUS DISSEMINATUS ACUTUS IN A PATIENT WITH SECONDARY SYPHILIS. Presented by DR. PAROUNAGIAN and DR. MASON.

J. Z., Polish, a restaurant employee, had had a genital sore six months previously, which he healed with applications of peroxide. On account of a sore appearing on the tongue, he applied to the throat department, from which he was referred to the syphilis clinic. A Wassermann test revealed a ++++ result and he was placed under treatment. From Aug. 18, to Sept. 24, 1925, he received six injections of silver arsphenamine and six injections of mercuric salicylate. On September 29, an eruption was noticed, most marked on the face, which at first was suspected to be an arsphenamine dermatitis. A more thorough history and examination excluded dermatitis, and the diagnosis was made as presented. The patient stated that the duration was of about six days. He gave a history of sea-bathing followed by sunburn. The lesions were profuse on the face and neck but scarce on the body.

LUPUS ERYTHEMATOSUS DISSEMINATUS. Presented by DR. BECHET.

J. K., a man, aged 54, an American said that ten months previously he had noted a bright red patch on the nose and adjacent regions, which soon became scaly and thickened. A few months later, similar patches appeared on the upper arms and neck. When he first appeared in Dr. Aitken's service, the face, neck and upper arms were covered with large, scaly, violaceous red, sharply defined patches with enlarged patulous, plugged, sebaceous openings. The patches on the arms showed little infiltration, but were scaly, sharply defined and the same violaceous red. The chest was entirely free. Through some misunderstanding, the face and neck were exposed for a considerable time to the air cooled quartz lamp, the chest being unprotected. In a few days, the patient developed a marked actinic dermatitis over most of the upper part of the chest, which did not subside in the usual way but on the contrary, soon assumed the characteristics of a patch of disseminate lupus erythematosus occupying the entire area of the upper half of the chest.

The case well illustrated the occasional extension of the disseminate type of lupus erythematosus following the application of strong actinic light, either

natural or artificial, on previously healthy skin, and proved that in the disseminate type of the disease actinic light could have a deleterious effect and should be used with caution, if at all.

DISCUSSION

DR. WISE: There are a number of cases of lupus erythematosus disseminatus presented at this meeting, and I think that it might be well to discuss the subject mainly from the angle of prognosis and treatment. Textbooks state that such conditions are almost invariably fatal; but, as a matter of fact, not so many fatal results are seen as might be expected. The subjects are not always followed up to the final outcome, but reported deaths are not frequent in this city. One such patient, on being asked how he felt, replied that he felt pretty well aside from the skin trouble, and he did not complain of any particular indisposition. Of course, that does not mean anything as to his future condition; but careful physical examination of many of these patients reveals no visceral diseases, and many of them apparently recover.

DR. BECHET: The patient that I present is shown to illustrate the untoward effects which actinic light occasionally causes in disseminate lupus erythematosus. The man had no lesions on his chest before treatment, yet after a strong dose of alpine sun he developed a severe erythema, which a few weeks later developed into characteristic lesions of disseminate lupus erythematosus. The case serves as a warning against the use of actinic light in the disseminate variety of the disease. In chronic discoid lupus erythematosus of the face, however, the compression method with the water cooled lamp is an efficient mode of treatment, and I have not observed any deleterious results from its application.

DR. SCHEER: I agree with the statement made by Dr. Bechet in regard to the deleterious effect of light in cases of lupus erythematosus; even in a discoid case it is not without danger. Last summer, a woman with discoid lupus erythematosus of the face went to the mountains and exposed the lesion to the direct sunlight; this was followed by a lupus erythematosus over her face, neck and the exposed part of the chest, and within a few months she died at Mount Sinai Hospital. In another case with a similar history, the patient died with symptoms of septic pneumonia, but no necropsy was made. It is risky to expose these subjects with lupus erythematosus to light treatment, whether of the discoid or of the disseminated type.

DR. SCHEER: I do not agree with Dr. Wise, as I believe disseminated lupus erythematosus is a serious disease.

DR. ROSTENBERG: I have seen a case similar to those reported by Dr. Scheer. A young girl with two or three discoid lesions on the face, was exposed to an erythema dose of the alpine lamp, and soon after the erythema subsided she developed new lesions in that area. I therefore object to using any strong light in lupus erythematosus.

My experience with lupus disseminatus is not so grave as in many reported cases. One of my patients who was shown at a section meeting last year exhibiting an extensive type of lupus erythematosus and also suffering from pulmonary tuberculosis, was treated with tonics and small doses of thyroid extract. She reappeared a few months later, with the skin condition almost healed and in much better health generally.

DR. ABRAMOWITZ: Cases of localized lupus erythematosus sometimes become disseminated with other treatment. Such instances have been recorded after tuberculin therapy and with the Hollander method of treatment. It is probably in the nature of a provocative reaction. I cannot see why the action of the ultraviolet ray (alpine lamp) cannot be regarded in a similar way. In my opinion, one should confine the ultraviolet ray treatment of these subjects to the lesions themselves and not expose the body; in the acute disseminated cases the alpine light should be omitted until more is known about its action.

DR. CANNON: I agree with Dr. Wise that the fatal cases of lupus erythematosus disseminatus are rather infrequent. The *Johns Hopkins Bulletin* reported the cases of three patients who died from an intercurent disease; in two cases, necropsies were held; tuberculous glands were found in each instance and tubercle bacilli in one. As for the use of the alpine light in cases of lupus erythematosus, I think it beneficial if carefully given. Treatment for the lesions themselves should be given first, and then generalized treatment should be tried, beginning with small doses. I have followed Barber's outline of treatment in two patients, that is, generalized alpine light, colon irrigations and injections of peptone, and I obtained decided improvement in both instances.

DR. MCCAFFERTY: Recently, I saw some patients with lupus erythematosus in Berlin, who were treated with a gold preparation and who showed good results. Has any one here ever seen any conditions of this nature in which the patients were so treated, and, if so, what results were obtained?

DR. WISE: I had a peculiar experience with a patient, a woman, with lupus erythematosus of the discoid type on the face and a marked adenitis of the neck; no treatment was given to the lupus lesions, but the enlarged glands were exposed to roentgen rays filtered with 3 mm. of aluminum. The patient developed lupus erythematosus over the exposed areas only, although she had never had lupus erythematosus of the neck before the roentgen-ray treatment was administered to the enlarged glands.

The Finsen Institute of Copenhagen, at certain intervals, sends out reports of cured cases of lupus erythematosus. All patients with lupus erythematosus, before they are exposed to the ultraviolet rays, should have a test treatment on the forearm or thigh, to find out whether they are hypersusceptible. If the patient develops an inflammation which persists, and which later assumes the character of fine lupus erythematosus after the redness from the treatment has subsided, it would be unwise to treat that patient with light; but a certain proportion of these subjects do not react in this unfavorable way, and with them the ultraviolet light is probably the ideal treatment.

PITYRIASIS ROSEA: ANAL CHANCRE: EVIDENCES OF CONGENITAL SYPHILIS. Presented by DR. PAROUNAGIAN and DR. MASON.

V. L., a man, aged 21, born in Spain, a laundry employee, was admitted for treatment on Sept. 28, 1925, with a history of sexual perversion. He said that the anal sore was of three days' duration. The glands below Poupart's ligament were markedly enlarged.

Examination revealed a salmon colored macular eruption confined to the trunk, which itched considerably and was of six days' duration. The patient had a high palate, arch, tubercle of Mibelli and an imperfect hair line.

PEMPHIGUS. Presented by DR. RULISON.

I. S., a Russian Jew, aged 30, married, who had a wife and one son living and well, and whose family history was unimportant, except that one brother had died at the age of 13 of diabetes, had had no pertinent illnesses, with the exception of influenza in 1918. In June, 1905, he had "caught cold" in the eyes; then blisters had appeared in the throat and under the teeth. He was told that he had pyorrhea, and two teeth were extracted. Early in September, blisters, sores, and boils began to appear on the skin. There had been difficulty in eating since July because of the sores in the mouth and throat, and the patient had lost 20 pounds (9 Kg.).

Lesions of pemphigus were present on the conjunctivae, buccal mucosa, and on the skin of thetrunk and extremities. They were most numerous in the mouth and on the elbows, knees, sacrum and legs. The patient's Wassermann test was negative. Examination of the heart, lungs, abdomen and genitalia had shown nothing abnormal.

TUBERCULOUS ULCERS. Presented by DR. ROSTENBERG.

P. G., a man, aged 35, American, dated his trouble back to an injury received during the war, for which an operation was performed. After the operation, he developed a right-sided hemiplegia, from which he recovered, except for a slight facial palsy. The blood and spinal Wassermann examinations made at that time were negative. About eight months prior to presentation, his right knee began to swell, and a "tumor" was excised. On examination, this "tumor" was found to be tuberculous. The skin wound did not heal, and the patient was referred to Dr. Rostenberg in July. He then had three distinct ulcerations, each from 4 to 5 cm. in diameter, having a punched-out appearance and a discharging base with soft reddish-blue borders. These healed promptly under five quart-lamp treatments. The ulcer shown on the left leg started about five weeks before presentation, the skin becoming red and the deeper tissues infiltrated, breaking down after a few days and assuming the size presented. An injection of arsphenamine given about two weeks before presentation had no influence on it, so the patient was again under treatment with the quartz lamp.

A CASE FOR DIAGNOSIS: SMOOTH ATROPHY OF THE TONGUE WITH BULLOUS LESIONS. PHENOBARBITAL RASH? PEMPHIGUS ORIS? SYPHILIS? Presented by DR. MAX SCHEER.

Mrs. A. H., (from the department of dermatology and syphilis, of the Vanderbilt Clinic), aged 37, white, suffered from attacks of painful lesions on the tongue for the past two years. The anterior half of the tongue showed well marked, smooth atrophy the surface was glazed and shining, and papillae were absent. In the atrophic area were a few pearl-like elevations, about the size of a pinhead. On the middle of the dorsum of the tongue was a verrucous lesion ¾ by 1 inch (1.9 by 2.5 cm.) in size. At the time of her visit to the clinic there were two bullous lesions on the under surface of the tongue, a linear one one-quarter inch (0.6 cm.) long and a round one one-quarter inch in diameter. These had disappeared at the time of the presentation. The Wassermann test was negative. No blood count was made. The patient said that for the past two years she had been taking a "nerve" medicine irregularly. Syphilis was ruled out by the negative Wassermann test and the presence of bullous lesions. There were no lesions on the skin. The drug history suggested the possibility of a phenobarbital rash.

DISCUSSION

DR. WOLF: I saw a patient who had taken phenobarbital for epilepsy, and who presented the triad of symptoms illustrated in Dr. Scheer's case.

DR. ABRAMOWITZ: Has the patient been given a dose of phenobarbital to determine whether the condition would break out again?

DR. SCHEER: The patient came to the clinic complaining of a sore tongue, which she had had for two years. At first glance, the condition suggested a tertiary syphilitic glossitis (smooth atrophy of the tongue); however, the Wassermann test was reported negative and there was no evidence of tertiary syphilis. At the time of her visit there were on the under surface of the tongue two bullous lesions, which would rule out syphilis. All that could be learned from closer inquiry was that she had been taking a nerve medicine for two years, but she could not tell what it was, possibly a bromid or phenobarbital. Pemphigus oris was the alternative diagnosis. There were no other lesions on the skin or mucous membranes.

Repeated attacks of glossitis from phenobarbital may cause a smooth atrophy of the tongue similar to that seen in syphilis. No test had been made by giving the patient phenobarbital, as she had not returned to the clinic.

LEPROSY? PSORIASIS? Presented by DR. ABRAMOWITZ.

Mrs. A. G., (from the department of dermatology and syphilis, of the Vanderbilt Clinic), Italian, aged 35, said that when she was 14 years old, a white spot appeared on her forehead. This spot became red and spread from the point of appearance to the eyebrows, from which the hairs fell out. As presented, the skin of her face was pale red, felt rather thin and velvity, with all hairs on her face absent. The trunk and lower extremities presented large and smaller plaques, some of which contained lesions of a follicular nature. The plaques had a distinct border, with a clearing center, and were slightly erythematous and somewhat infiltrated. Areas of marked pigmentation were present, especially on the lower extremities. The skin of the upper part of the chest was like that on the face, rather shiny, pinkish, and velvety. Numerous nasal smears were negative for Hansen's bacilli. The sensory tests were normal. The Wassermann test was negative. The first biopsy showed no parakeratosis, but a simple perifollicular inflammatory process. The report of a second biopsy was of a similar nature.

DISCUSSION

DR. POLLITZER: I think the lesions in the torso suggest psoriasis, but there is nothing absolutely characteristic on which one can make a positive diagnosis; against that diagnosis, however, is the appearance of the upper part of the woman's face. There is no keratosis; there is a diffuse infiltration; the skin is thick, smooth and red, and with that there is a loss of eyebrows, so that the whole picture is strongly suggestive of leprosy, although one would hesitate to make that diagnosis on the rather uncertain data. However, the diffuse infiltration of the upper part of the face, the loss of the eyebrows, and the superficial, circinate, irregular pigmented patches on the body are all somewhat in favor of leprosy, and I know of no other conditions which all these symptoms would fit.

DR. WISE: Might there not be two independent conditions?

DR. POLLITZER: Dr. Wise's suggestion is certainly tenable, but it is far more likely that the two kinds of lesions have a common etiology, and leprosy is capable of producing both of these lesions.

DR. ANDREWS: It would be interesting to make a microscopic examination. The condition might be an ordinary tinea versicolor, although not typical. It is a superficial, finelly scaling fawn-colored eruption that is slightly suggestive of a fungus infection.

DR. WOLF: I am inclined to think that it is parapsoriasis rather than Hansen's disease, and the lesion on the forehead is an independent condition based on endocrine dysfunction. So long as we do not know what parapsoriasis is due to, it might be classified with the dysfunctions of the endocrine system. Hansen's disease is ruled out because certain features are lacking: absence of infiltration in the lesions, no ulnar nerve thickening and no atrophy. On the other hand, favoring parapsoriasis, the woman has symptoms that fit in with that disease, namely, the superficial scaling erythematous nonitching eruption of a diffuse type.

DR. WISE: Dr. Andrews, I note that examination of the patient in daylight does not suggest tinea versicolor.

DR. ABRAMOWITZ: The patient was presented last spring by Dr. Graham at a meeting of the Brooklyin Dermatological Society, and most of the members then favored the diagnosis of leprosy. She was referred by Dr. Graham to the Vanderbilt Clinic, where Dr. Wise and I saw her. Several smears for leprosy bacilli then were negative. It is no surprise that the biopsy report indicates a mild follicular inflammation, for many of the lesions on the back are follicular. I have seen patients with pityriasis rubra pilaris that presented such a clinical picture in the period when the eruption was progressing. Some of the lesions resembled parapsoriasis en plaque.

A CASE FOR DIAGNOSIS. Presented by DR. GOODMAN.

M. S., a woman, aged 37, married, who had three healthy children, first presented herself at the hospital in April, 1923, with a scaly condition of the scalp. Ten per cent hydrargyri ammoniatum was prescribed and was refilled once. The patient did not return until July, 1925, when she presented an eruption of the trunk and extremities. The condition had been present for about six months, and the patient complained of itching. The patches were coin sized and shaped, ranging from the size of a quarter to that of a silver dollar. The lesions were rather symmetrical; the borders were not raised; the centers were somewhat rose colored and scaly; no infiltration was felt. A piece of one of the lesions was removed and sectioned, but the findings were not conclusive in that a pathologic diagnosis could not be given.

DISCUSSION

DR. POLLITZER: My impression is that it is a seborrheic dermatitis.

DR. WISE: It is unfortunate to dispatch the subject without further discussion; if the condition is a seborrheic dermatitis it should respond to treatment. What form of treatment has the patient had? From the history, it is difficult to draw any definite conclusions as to the nature of the case. The presenter said that the lesions would not respond to treatment; did she simply use calamine lotion for two or three days? It would be advisable to have the patient presented again with a more definite history, giving details as

to the treatment prescribed and as to the manner in which the treatment was carried out. Possibly a vigorous inunction of weak chrysarobin ointment would cause the lesions to vanish.

DR. GOODMAN: I can add little to the history as given in the presentation. The treatment has been lotions for applications externally, and the patient complained that she obtained no relief from them. The feature that particularly interests me is the possibility of the eruption being one of premycosis fungoides. I do not agree that a diagnosis of dermatitis seborrheicum is satisfactory. The lesions are not in the location of that eruption; there is no greasy scaling and no indefiniteness to the borders. Of course, the diagnosis of parapsoriasis had to be considered, but the scaling does not appeal to me as suggesting that, although the distribution of the lesions and their conformation was not unlike parapsoriasis. The feature of itching is also important. A mycotic infection is not considered. The borders of the patches do not show any vesiculation, nor is there any peripheral heaping of the scales. Had the pathologic picture of the microscopic section been of value, it would not have been necessary to present the patient for diagnosis.

DERMATITIS LICHENOIDES CHRONICA ATROPHICANS. Presented by DR. ELLER.

C. P., (from the department of dermatology and syphilis, of the Vanderbilt Clinic), a woman, aged 53, American, presented a condition with which she had been troubled for a year. There was an atrophic patch at the acromial end of each clavicle, also erythematous scaly patches at the flexures of the elbows, patches the size of a quarter at the inner side of the right breast, a patch 8 by 4 cm. at the upper left scapula, a patch the size of half a dollar over the right dorsal spine of the ilium, a palm-sized, scaly patch over the right buttock, an erythematous, scaly patch at the flexure of the knee, and a patch developing above the left ilium. The epigastrium showed atrophic white skin with scaly centers and follicular plugs. The elbow and knee flexures were somewhat lichenified. Pea-sized, slightly yellow infiltrating patches were developing, over which the skin was easily movable. Some were of the xanthoma type, others like morphea. There were isolated papular lesions at the bend of the elbows. The Wassermann test was negative. The biopsy report was: chronic dermatitis, lichenification and atrophy.

DISCUSSION

DR. POLLITZER: I suggest that my colleagues all read Czilak's description of this disease in the Jacobi Atlas. The subject just shown is a perfect reproduction, so far as the appearance of the lesions is concerned, of the patient described by Czilak. As to what that disease was that was another matter. A few years ago, I had occasion to observe a patient whom he studied histologically; the condition had all the earmarks of a scleroderma, and I have no doubt that dermatitis lichenoides chronica atrophicans belongs in that group.

ADENOMA SEBACEUM. Presented by DR. ANDREWS.

L. A., a boy, aged 13, of Russian birth, who had lived in the United States for ten years, had an eruption that was of gradual development since infancy. He presented pinhead to split-pea sized yellowish and pinkish papules, associated with dilated superficial capillaries symmetrically distributed over the nose, cheeks and nasolabial folds. At the center of the forehead was a verrucous

nevus the size of a silver dollar. The child was in Grade 8A, which represents a normal intellect of his age. The left side of the face had been treated with endothermy, and the lesions had been completely eradicated without scarring. The right side of the face was untreated and presented a contrast with the treated side.

SUBCUTANEOUS NODULAR SYPHILODERM. Presented by DR. PAROUNAGIAN and DR. MASON.

Mrs. M. M., aged 49, Irish, a cleaner, was admitted to the clinic Aug. 14, 1925. Venereal history was denied. She said that she had three living children and had had one stillbirth and two miscarriages. She presented lesions on the elbow, forearm, and dorsum of the right hand which were of nine months' duration and which were not painful. On two occasions the Wassermann examination was reported ++++. On September 14, she was given an injection of mercuric salicylate, which was followed by marked improvement. Active treatment was discontinued until after the presentation.

LUPUS ERYTHEMATOSUS LABIALIS. Presented by DR. CANNON.

H. T., a man, aged 22, American, presented lesions on the tip of the nose and on both lips which had been present since the age of 12. The lesions showed slight atrophy, with marked follicular openings. The skin of the upper lip showed less telangiectasis and more atrophy. The telangiectasis was more marked on the vermilion border until the mucous membranes were reached. There was mild scaling and erythema of the lower end of the ears. There was a mild geographic tongue. The patient gave a history of sensitiveness of the skin to sunshine.

DISCUSSION

DR. POLLITZER: When I inquired, the boy said that he had had the condition since infancy. He hoped Dr. Cannon would look into that point; it ought to be verified, for a lupus erythematosus of the lips since infancy would certainly be extraordinary.

DR. CANNON: The boy gave the history of having developed the lesions since he was 12 years old.

ANNULAR SYPHILODERM, SUPERFICIAL SYPHILITIC GLOSSITIS, REMAINS OF CHANCRE ON LEFT LABIA MAJORA. Presented by DR. PAROUNAGIAN and DR. MASON.

M. S., a negress, aged 22, married, born in the British West Indies, applied at the clinic on Oct. 2, 1925, for the relief of headache. She presented the following lesions: Remains of a chancre on the left labia majora; condylomas about the anal region; circinate lesions on the forehead and chin; mucous patches in the throat and a marked superficial glossitis resembling "geographic tongue." She gave an indefinite history; she thought the lesions of the face were of about a month's duration; she did not know that she had sores on her tongue, and did not complain of sore throat; she complained only of headaches.

SCLERODERMA. Presented by DR. SCHEER.

A. G., (from the department of dermatology and syphilis of the Vanderbilt Clinic), an embroideress, aged 21, first noticed the change in her skin two years before presentation. There was the typical board-like hardness on the

outer sides of the arms and on the cheeks. The circumoral region was free. The patient said that the skin had improved a great deal since the administration of thyroid extract.

DISCUSSION

DR. MCCAFFERTY: I read an article by a French investigator, in which the author reported a few cases of scleroderma which were treated with the alpine light. No other medication was given, and recovery was reported.

DR. LUDWIG WEISS: In the treatment of scleroderma I have had good results with thyroid extract. I presented a case at the Manhattan Dermatological Society a few years ago, which has since been quoted frequently. The patient was a young girl, with a band of scleroderma running obliquely over the forehead, which yielded to small doses of thyroid extract, a dosage of 1/6 of a grain (0.01 Gm.) continued for months. If the patient under discussion had an ovarian dysfunction, he would recommend the use of lutein added to the thyroid therapy.

CHANCRE OF UPPER LIP. Presented by DR. PAROUNAGIAN and DR. MASON.

Mrs. H. LaR., aged 23, who was referred to the clinic Aug. 19, 1925, then had had the lesion of the lip for three months. The incubation period was said to have been one month; the roseola was of the papular type and was not profuse. Her Wassermann test was ++++ on the date of admission. On Aug. 10, 1925, her husband presented himself, with a lesion of four days' duration, from which a positive dark-field examination was reported. His Wassermann test was negative on the first visit.

The patient received seven injections of arsphenamine and seven of mercuric salicylate from August 19 to September 30, inclusive, yet there was a considerable portion of the lesion remaining. No similar case with such resistance had been encountered.

DISCUSSION

DR. WISE: Dr. Fordyce presented a similar case, but on prolonged observation the condition turned out to be a keloid following a chancre. Dr. Parounagian's case, however, is not keloidal.

DR. PAROUNAGIAN: The lesion was much larger when first seen, but that as I have never seen a chancre of the lip so resistant to treatment, I presented the case. The treatment will be continued, and I shall report further on the case.

GRANULOMA ANNULARE. Presented by DR. CANNON.

This case was presented at a previous meeting. The patient recovered under injections of tartar emetic; then he had a recurrence and was treated again, made a second recovery, and has been well for three months.

DISCUSSION

DR. LEVIN: Have the inclusion bodies been found? Was the patient treated with vaccine?

DR. CANNON: The only treatment has been tartar emetic, and no inclusion bodies were found.

DR. WOLF: At the time of presentation, I inquired whether "if the case were cured with tartar emetic, the members of the section still would consider,

in the face of the pathologic diagnosis, that it was a squamous cell epithelioma?" Some of the physicians maintained that it was a squamous epithelioma, in spite of the fact that it cleared up under tartar emetic. I have a patient under observation, in whom the condition clinically is typical of squamous epithelioma of the tongue. A section was taken before radium was inserted, and the immense tumor on the dorsum of the tongue melted away rapidly. Although I felt sure that it was malignant, the report came back: chronic inflammatory tissue. The growth was almost the size of a walnut, and there were enlarged glands in the submaxillary region. That was another instance of discrepancy between the clinical and the pathologic diagnoses.

DR. PAROUNAGIAN: I can confirm Dr. Cannon's report of the condition as completely healed, with a good result. The man was a patient at Bellevue some time ago, and he also had a ++++ Wassermann reaction at the time. When seen recently, there was no evidence of any lesion, except a pigmented scar.

A CASE FOR DIAGNOSIS: BROCQ'S SYPHILID CORNÉE (?). Presented by DR. BECHET.

R. J., a negro, aged 36, had come to Dr. Aitken's service at the Skin and Cancer Hospital on the day of presentation. The eruption was located on both palmar surfaces, and consisted of hard horny patches and many acuminate horney processes extending deeply into the skin. These processes could be dug out, leaving pitlike depressions. There were many sievelike perforations throughout the patches. A specimen of blood had been taken for the Wassermann test. The lesions had been present for five years, and were limited strictly to the palms. They greatly resembled the condition described by Brocq under the designation syphilid cornée.

RECKLINGHAUSEN'S DISEASE. Presented by DR. SCHEER.

H. C., (from the department of dermatology and syphilis, of the Vanderbilt Clinic), a girl, aged 23, a typist, American, presented a generalized eruption of ten years' duration. There were a large number of soft papillomas scattered over the trunk, numerous lentiginous lesions over the back, and a few *café au lait* spots. Some of the larger lesions showed the characteristic hernia-like sacs due to loss of elastic tissue. There was no family history of the same disease. The patient was normal mentally.

SECONDARY SYPHILIS. Presented by DR. PAROUNAGIAN and DR. MASON.

J. M., aged 24, who had had a chancre on the prepuce two months previously, came to the clinic on Oct. 2, 1925, presenting a nodular and crusted eruption, most marked on the face, with similar scattered lesions on the body, and with condylomas about the genito-anal regions and between the toes of the right foot. The lesions were unusually severe. A Wassermann specimen was taken, but had not yet been reported on.

SECONDARY SYPHILIS; ANAL INFECTION; ALOPECIA SYPHILITICA; CONDYLOMAS OF THE UMBILICUS, TOES AND ANAL REGIONS. Presented by DR. PAROUNAGIAN and DR. MASON.

R. D., aged 18, was first seen on Sept. 10, 1925, presenting a fading roseola; mucous patches in the throat; condylomas about the umbilicus, anal regions and toes; marked swelling of the glands below Poupart's ligament; syphilitic

alopecia and a recent scar on the glans penis. The patient admitted frequent exposures as well as sexual perversions. The Wassermann examination revealed a ++++ reaction.

BLASTOMYCOSIS SHOWING RESULTS OF TREATMENT. Presented by DR. PAROUNAGIAN and DR. MASON.

J. K., aged 51, American, had been presented before the section with the diagnosis of blastomycosis. At that time the diagnosis was disputed, some favoring tuberculosis verrucosa cutis, others supporting the diagnosis as presented. The microscopic examination was not very enlightening.

During the early stages of the disease, wet applications of mercuric chloride, 1:10,000 were applied; later, mercurial ointment, 0.8 Gm.; ammoniated mercury, 22 Gm., and ascending doses of potassium iodide; and one application of roentgen ray was made. The lesion was practically healed.

SECONDARY SYPHILIS WITH SEVERE MANIFESTATIONS. Presented by DR. PAROUNAGIAN and DR. MASON.

W. S., aged 36, was admitted to the Bellevue Clinic on Feb. 21, 1925, having a frenal chancre. The dark-field and Wassermann examinations were negative. He received two injections of arsphenamine, and as the sore healed rapidly the patient considered himself cured and discontinued his visits. On Sept. 29, 1925, he returned to the clinic, presenting a generalized papular eruption, ulceration of the prepuce, extensive condylomas about the chin, anal region and the toes and mucous patches in the throat and on the tongue. The Wassermann examination was reported ++++ on September 29.

ANNULAR SYPHILID OF THE FACE: PALMAR AND PLANTAR SYPHILODERM: CONDYLOMAS GENITO-ANAL REGIONS AND NECK; ROSEOLA. Presented by DR. PAROUNAGIAN and DR. MASON.

W. W., a negro, aged 17, was seen on Sept. 28, 1925, but was unable to give a satisfactory history. He stated that for two months he had had phimosis; before this happened, he had noticed a sore at the sulcus. He had been exposed frequently. His Wassermann test was reported ++++. In addition to the lesions mentioned, he had numerous mucous patches on the tonsils, and bilateral inguinal adenitis.

SQUAMOUS CELL EPITHELIOMA OF THE LOWER LIP. Presented by DR. LEVIN.

N. C., a man, Italian, unmarried, aged 26, a longshoreman, had had a small growth over the left side of the lower lip nine months ago. This was excised by a physician four and a half months prior to presentation. It promptly recurred and was again removed two and a half months ago. The lower lip, near the left corner, showed a quarter-dollar sized irregularly rounded lesion with a hard, rolled, polished border. The central zone was ulcerated, and the floor was bright red and covered with tuberculous and papillary outgrowths.

ANAL SYPHILITIC INFECTION: PALMAR AND PLANTAR SYPHILIDS: CONDYLOMAS ANI AND TOES: FADING ROSEOLA: ENLARGED GLANDS BELOW POUPART'S LIGAMENT. Presented by DR. PAROUNAGIAN and DR. MASON.

T. M., aged 19, was admitted to the clinic on Sept. 23, 1925, with a history of sodomy. The last exposure was said to be about three months prior to presentation. The history of the duration of the lesions was vague, though the

following were observed when first seen: marked condylomas around the anal region and between the toes; a fading macular eruption; palmar and plantar syphilids; unusual swelling of the lymphatics below Poupart's ligament, and moist papules about the genitals. His Wassermann examinations revealed a ++++ reaction. The patient was of low mentality, and exhibited certain signs of congenital syphilis.

The presenters believed that the majority of perverts were congenital syphilitics.

Secondary Syphilis (Anal Infection); Leukoderma Syphilitica; Condyloma of the Anus, Penis and Scrotum; Evidences of Congenital Syphilis. Presented by Dr. Parounagian and Dr. Mason.

C. W., aged 18, a bus-boy, was admitted to the Bellevue Clinic on Sept. 28, 1925. He denied having had any sexual relations with women, but admitted perversion with men. His history was rather difficult to obtain on account of his low mentality. He believed the anal sores were of one month's, and the penile sores of three weeks' duration. Both parents were dead. His expression was dull; he had a high arched, palate, an imperfect hair line, and the teeth were suggestive of congenital syphilis. His Wassermann test on the day of examination revealed a ++++ result.

Geographic Tongue in a Patient with Congenital Syphilis. Presented by Dr. Parounagian and Dr. Mason.

Miss E. A., aged 22, an Italian-American, whose parents were patients at the Bellevue Clinic for three years, the mother having persistent ++++ Wassermann tests. The patient had interstitial keratitis for five months, and had received twelve intravenous injections at the Eye and Ear Hospital. She applied at the Bellevue Clinic on Sept. 4, 1925, complaining of constant headaches. Her Wassermann test was ++++. During the examination, the peculiar concentric patches which had existed since childhood were discovered on the tongue. She was presented mainly on that account.

Charcot's Knees. Presented by Dr. Parounagian and Dr. Mason.

Mrs. M. O., a widow, aged 60, Irish, referred by Dr. J. E. Sutton to Bellevue Clinic for the treatment of her knee-joint condition, which was said to be of four months' duration, had a negative personal history and negative Wassermann tests. She said that her husband had a ++++ Wassermann test, and that he died the previous spring of general paralysis. Examination revealed a marked swelling of both knees, the right being larger than the left. There was no sign of inflammation and the condition was not painful. The knee reflexes were absent. Because her blood Wassermann test was negative, she was given a provocative injection of silver arsphenamine on the day of admission (Sept. 30, 1925). On request, Dr. Sutton of Bellevue Hospital supplied the report of the roentgen-ray examination made September 18 which was as follows:

"Atrophic osteo-arthritic changes in both knee joints, the atrophy being somewhat more marked on the right side. Moderate effusion in both knee joints, and some effusion in the suprapatellar bursae. No disintegration of the cartilages. No masses in the knee joints."

It was presumed that the condition had not progressed to produce the amount of destruction which this disease is supposed to represent. Clinically, the condition was considered to be in the early stages of a Charcot's joint.

Oscar L. Levin, Secretary.

MINNESOTA DERMATOLOGICAL SOCIETY

Oct. 7, 1925

G. M. Olson, M.D., *Presiding*

Dermatitis Medicamentosa. Neurotic Excoriations. Presented by Dr. Sweitzer.

Miss F., aged 27, was nervous and was given both iodin and bromids. A drug eruption appeared on the back of her trunk and on the neck. The patient scratched the tops of the lesions and many pigmented scars resulted.

Actinomycosis. Presented by Dr. Sweitzer.

C. L., a man, aged 56, an engineer, married, said that the first lesion appeared on the buttocks about one year before presentation. The condition was diagnosed as a boil, and was opened by a physician. Numerous similar lesions appeared on the buttocks and on the lower part of the abdomen. He was treated at the University last spring. He was given potassium iodid by mouth at that time, and not much improvement was noted. The patient was later given sun lamp treatments by a physician, with some improvement. At the present time the patient is being given lamp treatments and sodium iodid intravenously; 1 Gm. every fourth day. Definite improvement has been noted. At present the patient shows numerous small indurated masses, draining sinuses, scars and thickened, reddened skin on the buttocks and lower part of the abdomen. Fungus was found.

DISCUSSION

Dr. Olson: Good results have been reported from rather large doses of thymol in actinomycosis. Large doses of thymol have been used in the treatment of hookworm disease, but some accidents have been reported, so that caution appears to be necessary.

Dr. Sweitzer: I think that I should use thymol. The patient has been receiving iodids, and is improving somewhat.

Erythema Multiforme with Lesions in the Mouth. Presented by Dr. Michelson.

A man, aged 27, who did hard outdoor work, said that he had had three attacks similar to the present one, and they had always occurred during the spring or fall. The present attack began five days before presentation, with itching of the palms and soles. He took a Phenolax tablet, and the next morning an eruption appeared on the forearms and legs. He took a second Phenolax tablet, and the eruption then became much aggravated. At the present time he had large erythematous plaques making perfect circles on the palms and soles. These lesions were 4 cm. in diameter. On the extensor surfaces of the forearms were similar but smaller lesions. The lesions were deep pink, made up of concentric rings, the center being lighter than the periphery. There were also lesions in the mouth, on the genitals and about the anus. The lesions on the mucous membrane were round, shallow ulcers, covered with a yellowish pedicle; those in the mouth were around the buccal surfaces of the lips and cheeks. All the lesions were painful to touch. The patient said that during the previous attacks he had not taken Phenolax, but that none of the previous attacks were as severe as the present one.

DISCUSSION

DR. GAGER: I believe this man is quite sick. He reminds me of an experience I had a number of years ago with a patient who looked a good deal like this man, with marked erythema multiforme. My patient told me that he had had previous attacks two years before during the spring and that his physician had rushed him to the hospital and had given him six injections of arsphenamine for syphilis. My impression is that these cases may be tuberculous, because my patient recovered from the erythema multiforme, and within four months had acute miliary tuberculosis and died within three weeks. Since then I have been handling these cases with a great deal more care than before. I believe Dr. Michelson's patient should be under observation for a time and be thoroughly examined and some care taken of his general health after he recovered from this attack.

DR. MICHELSON: These conditions are prone to recur at the same time during succeeding years. In a recent case I found a low hemoglobin content and gave the patient injections of iron and arsenic, and the lesions cleared up rapidly, I believe much faster than is the usual course for erythema multiforme.

A CASE FOR DIAGNOSIS (SCROFULODERMA GUMMOSA?). Presented by DR. MICHELSON.

A well developed girl, aged 13 years, who had enjoyed good health with only the usual childhood diseases, four months previously had developed a small pustule under the angle of the right jaw, her mother said, and this had gradually enlarged and had been opened as a boil. It exuded only a small amount of pus, and in four months had gradually enlarged but had not healed. At the time of presentation there was an ulcer measuring 3 by 2 cm. located under the ramus of the right mandible. The base was granular and covered with bits of necrotic tissue. The borders were definitely undermined and considerably raised. The amount of exudate was not great, requiring only a change of dressing every two or three days. The patient had been examined carefully by a competent pediatrist, who said that there was a suggestion of concealed pulmonary tuberculosis, but that he could make no definite diagnosis. No bacilli were found in the secretion. The patient had been subjected to two ten minute exposures of half strength radium plaque, applied with only gauze filter, and some healing appeared to be taking place.

LUPUS ERYTHEMATOSUS CONGESTIVE TYPE. Presented by DR. SWEITZER.

Mrs. C., aged 47, gave a history of having an eruption on her face and arms. The condition had been diagnosed as eczema and as acne rosacea. The face and the backs of the hands showed a swollen and reddened condition, which varied slightly from day to day. Biopsy showed slight squamous scaling, edema of the epidermis, marked round cell infiltration in the papillary portion and some follicular dilatation.

DISCUSSION

DR. GOECKERMAN: From what I saw of the patient, I would agree with the diagnosis. I am rather interested to know what type of eruption she has had on her face, since it is rather difficult by examination to know just what it had been. Did it resemble the type known as erythema faciei perstans? Has the patient pyrexia periodically?

DR. SWEITZER: I told the patient to remain in bed, and I diagnosed acute lupus erythematosus. Sometimes when the patient consulted me her face would be quite congested and sometimes not.

ADENOMA SEBACEUM (PRINGLE); NEUROFIBROMATOSIS (VON RECKLINGHAUSEN); PSORIASIS VULGARIS. Presented by DR. MICHELSON.

A young farmer, aged 26, said that he had had the condition on his face and back as long as he could remember, but that recently a scaling eruption had appeared on the scalp, arms and legs. Over the shoulders and back there were about 600 or 800 small, soft, pendulous, whitish tumors; the pedicle in most instances was very small, so that the tumors looked like flat seeds hanging by a stem. On the face, especially at the nasal folds, and over the forehead, there were small yellowish-red sessile papules, and a large number of vascular dilatations. The scaling eruption was typical of psoriasis vulgaris, and was present in the areas of predilection. Mentally, the patient was alert. He said that he had finished the first year in high school at the head of his class, and had stopped because of stress of circumstances.

DISCUSSION

DR. OLSON: This case resembled almost exactly one that I showed four or five years ago, except that this man is bright mentally while my patient was dull. If there is tuberose sclerosis of the brain, the patient shows mental defects. Some patients show extensive involvement of the skin with few if any lesions in the brain. Other patients with only a few lesions in the skin may have extensive tuberose sclerosis of the brain. Adenoma sebaceum may exist with lesions in almost any organ of the body, as the stomach, intestines, etc. There are often mixed cell tumors of the kidney. Genetically, these lesions are similar to the skin lesions. Some patients show a combination of adenoma sebaceum and Recklinghausen's disease.

LEUKODERMA FOLLOWING PITYRIASIS ROSEA. Presented by DR. MICHELSON.

A medical student, aged 19, had spent the summer in a camp, and the upper half of his body had constantly been exposed to the sun's rays. He was tanned to the color of a mulatto. Two weeks before presentation he noticed two or three white patches which developed about the waistline. Gradually the number of patches had increased, until the entire back and chest were covered with scaling lesions varying in size from 1 to 2 cm. in diameter. They were accompanied by slight itching. As the scaling and itching subsided, white areas corresponding to the size of the patches remained.

DISCUSSION

DR. GAGER: I consider pityriasis rosea an interesting condition. Dr. Michelson's case, for instance, is what the Vienna school calls pityriasis alba, which is seen commonly over there, as the people are more addicted to sun baths. Dr. Turnacliff's case appears to be pityriasis rosea in a seborrheic person. This condition sometimes differs in the same person according to different stages of irritation. This feature of the disease is interesting, and physicians in general do not appreciate the importance of the varieties of pityriasis rosea.

DR. MICHELSON: I agree with all that Dr. Gager has said, and I want to call attention to another point; that is, the variation in the length of time in

which pityriasis rosea runs its course. I believe that habits, such as bathing, occupation, type of clothing and muscular activity, have a distinct bearing.

DR. GOECKERMAN seconded what had been expressed; that one can get many rather bizarre pictures and that sometimes it took rather prolonged observation to reach a conclusive diagnosis. He had often observed cases of the unusual type that later proved to be typical. As the cases evolved, one could get a fairly classical picture. The factors brought out tonight are probably modifying factors.

A CASE FOR DIAGNOSIS. Presented by DR. GOECKERMAN.

The patient first noticed small "fever blisters" on the left side of the lower lip. These healed for a period, and then reappeared. For the last two months there had been a similar lesion on the upper lip and anterior to the left ear. Similar lesions had subsequently appeared on other parts of the face and recently also a few lesions about the umbilicus. Dr. Goeckerman said that they had observed this patient for five or six weeks, and their impression was that they were probably dealing with pemphigus, but they had not felt that they could make that diagnosis final. They had thought that on the palate they had seen small vesicles which were of a transient type. They had not seen any bullous lesions. With the exception of the possible vesicular lesions, there had been no other lesions than those presented by the patient. The lesions on the face had perhaps become more marked. The lesions around the umbilical region were rather recent. They had tried ordinary culture mediums and microscopic examinations repeatedly, but they had made no special examinations.

DISCUSSION

DR. SWEITZER: This condition is probably pemphigus. The patient resembles a patient I have at the hospital now who has pemphigus on the body. I have been using the Davis treatment for a couple of years and had good results at first, but these results were only temporary.

DR. GOECKERMAN: This patient has been on the Davis treatment almost as long as we have observed him, but so far he has not shown any response.

A CASE FOR DIAGNOSIS. Presented by DR. SWEITZER.

A man, aged 29, presented a circinate plaque on the back of the tongue. The anterior part of the lesion was level with the surface, but seemed indurated. The posterior part of the lesion was slightly elevated. A few discrete glistening papules were present on the right pillar. The patient denied venereal infection. The Wassermann test was negative.

DISCUSSION

DR. SWEITZER: I am inclined to make a diagnosis of syphilis as the patient has received intravenous injections of neo-arsphenamine and is improving. I should continue this treatment.

LYMPHEDEMA OF BOTH LEGS. MILROY'S DISEASE. Presented by DR. SWEITZER.

H. R., a young man, aged 20, had a chronic enlargement of both legs. The condition started in early childhood and was slowly getting worse. His father also had the same condition but in a more severe form, with greater enlargement.

The feet were swollen and the ankles enlarged giving the leg a round appearance. The swelling was firm in consistency.

The patient complained of numerous boils and subcutaneous abscesses which probably were caused by the lowered resistance of the skin from the chronic edema.

The condition was a chronic lymphedema or Milroys' disease.

DISCUSSION

DR. SWEITZER: This is the second case of Milroys' disease shown before this Society. Dr. Michelson presented one case.

DR. MICHELSON: This interesting condition was originally described by an American. It is distinctly familial in type, and it may occur in either one limb or in both limbs, and in either sex. No treatment has been of much avail, although surgical treatment has been tried.

HYPERTROPHIC SCARS. Presented by DR. SWEITZER.

Mr. F., aged 67, had herpes zoster three or four years before presentation. About a year and a half ago, a small tumor appeared at the site of the former zoster. This spread until an area about the size of a hand was involved. The central parts involuted, according to the history. The patient presented a circinate, smooth tumor, firm to the touch. The lesion was located on the scapular region and on the side of the chest. The center of the area showed pigmentation but no tumor. Biopsy showed hypertrophic scar tissue and superimposed inflammation.

DISCUSSION

DR. SWEITZER: This is a puzzling case. When I first saw the patient he gave a history of these tumors which had involuted. He spoke of the possibility of a mycosis fungoides or a leukemia. Dr. Michelson had made a biopsy and found that the lesions apparently were hypertrophic scarring. This is the first case of this kind that I have ever seen following herpes zoster. I have seen many cases of herpes zoster, but no scarring after one of them.

DR. OLSON: I have seen keloid following herpes zoster, especially in elderly people.

D. D. TURNACLIFF, M.D., Secretary.

PHILADELPHIA DERMATOLOGICAL SOCIETY

Regular Meeting, Oct. 12, 1925

JOHN H. STOKES, M.D., *Presiding*

PITYRIASIS ROSEA. Presented by DR. GREENBAUM.

A. M., a colored woman, aged 30, presented a generalized eruption of papules and scaly patches, of six days' duration. It was generalized except on the face and parts below the knees. She had some lesions on the palms. Itching was marked. The result of the Kahn test was plus one. She was presented for confirmation of the diagnosis.

DISCUSSION

DR. WEIDMAN: I believe that the underlying dermatosis was masked by treatment.

DR. HIRSCHLER: I agree with Dr. Weidman, and suggested that in view of the rapidity of development of the lesions, it may be an acute erythematous rash. I think that although the larger lesions show irritation, the condition is rather suggestive of pityriasis rosea; however, the neck is a rather unusual location for the first patch.

DR. GREENBAUM: Follicular syphilid must be excluded. Six cases in negroes were seen during the last year, and at times the condition was scaly and intensely itchy. It is my opinion that the case presented is one of pityriasis rosea modified by sulphur treatment.

DR. STOKES: I would call attention to the seborrheic distribution, but I agree with the diagnosis.

RECURRING HERPES SIMPLEX. Presented by DR. SIDLICK.

A. S., a white girl, aged 14, presented a number of vesicles in the palms. The vesicles were circumscribed with an inflammatory areola. The condition had been recurring for the past five years in the same location on the palms.

DISCUSSION

DR. STOKES: I should like to have therapeutic suggestions on those obstinate lesions.

DR. WRIGHT: Were the lesions examined for mycelia?

DR. SIDLICK: Prior to the eruption each time, there was an itching and a tingling sensation. The vesicles were examined for mycelia, but none was found. The content of the vesicles was a clear fluid.

DR. GREENBAUM: In making an absolute differential diagnosis, corneal inoculation in a rabbit should be employed. When the lesions are those of recurring herpes simplex, a severe keratitis is the result. In cases of recurring herpes simplex I have been successful with the roentgen ray as a therapeutic measure.

DR. HIRSCHLER: I should advise tonic treatment in a child of this type, because the whole tone of the body is below par. I should recommend cod liver oil and a soluble iodin in small doses.

TUBERCULOSIS OF THE TONGUE. Presented by DR. WEIDMAN.

A. G., aged 39, a white man, appeared last February, complaining of the nodule on the left side of the tongue. There was a dense scarlike infiltration on the left side of the tongue, extending also on the floor of the mouth. There were also some circumscribed lesions which were punctured; and material obtained was examined, but no tubercle bacilli were demonstrated. Numbers of cocci were present. Nose and throat specialists reported that the larynx was scarred and the vocal cords bound down by adhesions as if burned. There was left submaxillary glandular enlargement. This was a month after the patient had drawn some paint remover into the mouth. There was a question as to the cause of the disturbance in the larynx, the paint remover being questionable. The Wassermann test was negative three times, one being provocative. The sputum was negative. Carcinoma was excluded by biopsy. Clinically

the differential diagnosis lay between tuberculosis and syphilis. A second biopsy was performed with guinea-pig inoculation. Acid-fast bacilli were demonstrated.

DISCUSSION

DR. WEIDMAN: From simple clinical appearances, the lesion seemed to be gummatous or carcinomatous. The amount of fibrous tissue was rather against a tuberculous process of only eight months' duration. Roentgenograms of the chest showed lesions of the lung.

DR. AHLSWEDE, Hamburg, Germany: I think that the paint remover had nothing to do with the lesion, although it might have created a locus minoris resistentiae.

DR. WEIDMAN: It is more common to find the ulcerative tuberculosis of the tongue than the type with fibrosis. The large masses in the case presented look more like abscesses than they look like the caseous material of tuberculosis.

DR. STRAUSS: I cited a similar case at the Jefferson Hospital three years ago, in which the patient did very well locally under radium treatment. In this case the right lung is riddled with tuberculosis.

DR. WEIDMAN: I remember the case as one of the proliferative type. The case presented is more of an interstitial glossitis.

DR. STRAUSS: I have used ultraviolet light in only one case with perfect results and little scarring, but the tuberculous process involved only the larynx.

DR. STOKES: I believe the combination of arsphenamin and ultraviolet light gives the best results in tuberculosis. Effort should be made simply to induce a gradual tanning of the patient using a suberythematous dose, gradually increased.

A CASE PRESENTED FOR DIAGNOSIS. By DR. STRAUSS.

J. S., a man, aged 28, was first seen on presentation at this meeting. He had a lesion on the side of his face of five weeks' duration. This lesion was whitish, oval, with a slightly elevated border and depressed center.

DISCUSSION

DR. SIDLICK: The appearance of the lesion and the history available are in favor of the diagnosis of morphea.

DR. CORSON: I do not agree with that diagnosis — there is not the white lardaceous color, and the border is a little too much raised. I do not venture a diagnosis.

DR. WEIDMAN: My diagnosis is granuloma annulare. Granuloma annulare in this same position was reported in the "Journal of Cutaneous Diseases." I exclude morphea because that lesion extends peripherally from the center.

DR. STOKES: I agree with Dr. Weidman, but I should like to have a biopsy report. I have seen erythematous lupus in a person with this kind of a lesion.

DERMATITIS HERPETIFORMIS. Presented by DR. BROWN.

C. M., a woman, aged 45, had an eruption limited to the legs, of three months' duration. There was a tendency to grouping with small vesicles which disappeared, leaving intense itching. The case was presented because of the limitation of the eruption.

DISCUSSION

DR. BROWN: A blood sugar test was not made, but the urinalysis was negative for sugar.

DR. WRIGHT: If the legs were painted with a coat of glycero-gelatine jelly it would serve four purposes—the air would be kept out and itching might cease; the patient would be unable to excoriate the skin; the present lesions would heal and the veins be supported.

DR. BROWN: The suggestion of dermatitis factitia was made, but the clusters were not linear and the lesions were too inflammatory for a factitial origin, although scratching had undoubtedly made them worse.

XANTHOMA TUBEROSUM. Presented by DR. WRIGHT.

A. G., a white man, aged 47, had lesions of four years' duration, on the elbows and fingers. There were groups of pea-sized, yellowish soft tumors. A diagnosis of xanthoma tuberosum was made. Blood cholesterol determination showed 410 mg. (The normal variation is from 180 to 210 mg. per one hundred cubic centimeters of blood.)

DISCUSSION

DRS. WEIDMAN and STOKES agreed to the diagnosis of xanthoma tuberosum.

DR. STOKES: Was the patient's diet regulated?

DR. GREENBAUM: Hypercholesterolemia is not always present in xanthoma, and the cholesterol metabolism is not always upset during the course of a case of xanthoma. In a case that I previously reported, the blood cholesterol was normal, and the patient was fed 3 ounces of cholesterol a day over a period of three months, without any effect on the blood cholesterol. This meant to me either that hypercholesterolemia has nothing to do with xanthoma, or the mechanism of cholesterol metabolism adjusts itself, and the individual is spontaneously cured. In the case now presented there is danger of recurrence in situ if the xanthoma is destroyed by fulguration, as the cholesterol metabolism is upset.

DR. SIDLICK: Is not cholesterol, even in abnormal amounts, deposited in the tissues?

DR. WEIDMAN: There is possibly another explanation of our failure to detect the excess of cholesterol, that is, the existence of cholesterol in another form. There are a number of different cholesterol bodies: oxycholesterol and isocholesterol, and one or two other forms which vary particularly in relation to their solubilities. In the negative cases it is our duty to determine the form of the fatty substance in the lesions on the body—but there are other fats and soaps besides cholesterol in the lesions, and the subject is not exhausted until examination is made for these also.

ARSENICAL KERATOSES. Presented by DR. WRIGHT.

L. N., a white man, aged 44, had marked arsenical keratoses on the palms and soles after taking arsenic for seven years for psoriasis. The psoriasis was of fifteen years' duration, and had covered him from head to foot. It was in a fairly good state when presented.

DISCUSSION

DR. BROWN: I think it is a mistake to treat psoriasis with arsenic, as the patient is exposed to the risks of arsenic poisoning without assurance that he will be cured of the psoriasis.

DR. AHLSWEDE: There should be a way of stopping the sale of liquor potasii arsenitis (Fowler's solution) on old prescriptions.

PHENOLPHTHALEIN POISONING. Presented by DR. SIDLICK.

M. S., a white man, aged 28, had been taking laxatives since childhood. Recently he had an eruption induced by the taking of phenolphthalein, and when that rash disappeared, it was deliberately induced a second time with that drug. There was a circumscribed eruption limited to the hands and face.

DISCUSSION

DR. SCHILDKRAUT: I saw such a case recently, but the patient had a permanent pigmentation at the site of the eruption.

CARROLL S. WRIGHT, M.D., Secretary.

DETROIT DERMATOLOGICAL SOCIETY

Regular Meeting, Oct. 20, 1925

HOWARD J. PARKHURST, M.D., *Presiding*

DERMATOPHYTOSIS OF THE SOLES WITH GENERALIZED DERMATOPHYTID. Presented by DR. JAMIESON.

B. S., a man, aged 47, a shipping clerk, presented a generalized eruption undergoing involution; it had been erythematovesicular. For twelve years there had been a typical dermatophytic eruption on the soles, with exacerbations in the summer. There had been an exacerbation a few weeks previously, followed by the appearance of a generalized, intensely pruritic eruption of small vesicles and papulovesicles. Treatment for scabies before the patient's admission to the hospital had been without avail, but appropriate treatment of the soles had been followed by prompt improvement in both the generalized and the local manifestations.

DERMATITIS EXFOLIATIVA. Presented by DR. JAMIESON.

C. W., a negress, aged 23, married, presented generalized desquamation, more profuse on the palms and soles. She had received arsphenamine injections two years previously, but none since that time. The eruption was said to have been present for four months, having begun as a group of itching papules on one thumb; it had gradually spread, with sensations of burning and itching. On the extensor surfaces of the forearms were a number of flat lichenoid lesions, and lichenification was pronounced in many areas.

ERYTHEMA MULTIFORME. Presented by DR. SCHILLER and DR. PERKINS.

Mrs. A. Z., middle-aged, of foreign birth, had noticed malaise five days previously, followed on the next day by a generalized eruption of macules

and papules from the size of a pinpoint to that of a half dollar; their color varied from purple to fawn, and some were hemorrhagic. They were described as painful.

DISCUSSION

DR. BIDDLE: Agreeing with the diagnosis, I would point out the fact that this patient has had repeated attacks of tonsillitis.

LUPUS ERYTHEMATOSUS AND SARCOID. Presented by DR. VAN RHEE.

Mrs. E. C., aged 31, a housewife, born in England, presented a small, coin-sized erythematous patch with a depressed center on the right cheek; this lesion had apparently been aggravated by the administration of Fowler's solution. On the right shoulder there was a medium coin-sized erythematous infiltrated patch. The Wassermann reaction was negative.

DISCUSSION

DR. BIDDLE: The patch on the face is typical lupus erythematosus.

DR. BREITENBACH: The infiltrated patch on the shoulder may be a sarcoid.

DR. JAMIESON: While the patient was in England, the diagnosis of lupus erythematosus in the facial lesion was verified by biopsy.

DR. KEIM: I agree with the diagnosis of lupus erythematosus for the lesion on the cheek with its central atrophy, and of sarcoid for the infiltrated patch on the shoulder.

VERRUCOUS LUPUS ERYTHEMATOSUS. Presented by DR. JAMIESON.

F. W., a Polish laborer, aged 36, had had an eruption for nine months, consisting of large erythematosquamous plaques symmetrically distributed over the nose, cheeks, ears and dorsa of the hands. The buccal mucosa was also involved. There was a distinct verrucous appearance in the patches, and the scales were adherent. The examination of the chest and teeth had been negative, except for the presence of marked pyorrhea. There had been considerable improvement following an injection of silver arsphenamine.

A CASE FOR DIAGNOSIS: LUPUS ERYTHEMATOSUS? Presented by DR. JAMIESON.

J. W., a man, aged 35, born in Poland, complained of soreness of the left faucial region, of several months' duration. He stated that while working at his occupation as a maker of automobile bodies, he held nails in his mouth constantly, and attributed the oral lesions to that cause. On the upper and posterior part of the soft palate, and on the left side of the uvula, there were areas of scarring and small coalescing superficial ulcerations. There was no surrounding inflammatory zone, and there had been little extension of the process during the previous two months. The Wassermann reaction was negative, as well as a therapeutic test for syphilis. The biopsy findings had not been conclusive. A tentative diagnosis of lupus erythematosus was offered.

FOX-FORDYCE DISEASE OF THE AXILLAE AND PUBES. Presented by DR. JAMIESON.

Miss E. H., aged 21, who gave no history of preceding eruptions, presented extensive pruritic patches of small follicular papules in the axillary and pubic regions. The patches had appeared rapidly one year previously, following furunculosis of the axillae.

FOLLICULAR PAPULAR SYPHILIDS. Presented by DR. WANDER.

A young man, with a recent syphilitic infection, in June, 1925, had first noticed the appearance of tiny papules, slightly elevated, and with a tendency toward grouping in small patches. The eruption was of general distribution, and the color was faintly erythematous to brownish. The skin was dry, and some scaling was present. There had been some loss of hair. The Wassermann reaction was strongly positive.

DISCUSSION

DR. JAMIESON: I cannot conceive of these lesions being purely syphilitic; there seems to be another factor, possibly seborrhea.

A CASE FOR DIAGNOSIS. Presented by DR. TROXELL.

J. M., a waiter, aged 24, American, had first noticed multiple vesicles on the arms and legs two months previously. It had gradually spread, involving the entire skin surface, except that of the face, hands and feet. There were bullae of various sizes, and some excoriated and crusted areas. Slight pigmentation appeared in the healing excoriations. The arms, legs and hips were especially involved. Ten days before the time of presentation, vesicles had appeared on the oral mucosa, causing little inconvenience to the patient. Severe pruritus had been quite constant. The Wassermann reaction was negative.

DISCUSSION

DR. BARTHOLOMEW: The case is one of pemphigus vegetans.

DR. BIDDLE: This case illustrates the difficulty of differentiating between dermatitis herpetiformis and pemphigus in some borderline cases.

DR. KEIM: In view of the marked systemic reaction in this case, I would favor a diagnosis of pemphigus.

DR. PARKHURST: The pigmentation, sites of predilection and pruritus favor a diagnosis of dermatitis herpetiformis, but pemphigus must be considered also.

DR. TROXELL: The appearance of oral lesions suggest the likelihood of pemphigus.

TRICHOPHYTOSIS. Presented by DR. SCHILLER.

Small and large areas of partial alopecia, crusting and scaling, were present on the scalp of a woman, as well as on that of her brother, her son and one other member of her family. The mother had had the condition for seventeen years. The family had recently immigrated from Europe.

DISCUSSION

DR. TROXELL: The patches give one the impression of folliculitis decalvans, although those on the children's scalps are suggestive of tinea.

DR. KEIM: The yellowish crusts are suggestive of favus.

DR. PARKHURST: I agree with a diagnosis of favus. The sparse growth of dry, wiry hair on the mother's scalp, with the underlying scarring, are quite characteristic of it.

DR. SCHILLER: The father, who was not presented, is said to have had the same condition for thirty years.

MULTIPLE BENIGN CYSTIC EPITHELIOMA. Presented by DR. STEVENS.

A woman of middle age presented, on the face and chiefly about the chin, numerous shiny pale elevations the size of a pinhead, which were said to have been present for several years. One on the chin was hemorrhagic in appearance.

Regular Meeting, Nov. 17, 1925

HOWARD J. PARKHURST, M.D., *Presiding*

A CASE FOR DIAGNOSIS. Presented by DR. ANDREW P. BIDDLE.

Mrs. M. L., aged 55, a housewife, had had a progressive, diffusely erythematous and infiltrated process for three months, involving the tip of the nose. Her husband had died of tabes.

DISCUSSION

DR. WILE: Although its evolution is remarkably rapid, I would consider this a case of rhinophyma. Soft and vegetating, it does not present the picture of nasal syphilis.

DR. KEIM: I consider this an unusual type of syphilitic eruption. However, if this lesion were on the leg, it would be diagnosed as bromoderma.

SARCOID OF BOECK. Presented by DR. ROBERT C. JAMIESON.

Mrs. M., aged 33, a housewife, presented several flat, infiltrated erythematous ill-defined patches on each cheek, adjoining the nose. They and similar lesions had been present at intervals for a year, having first appeared after a "growth" had been removed from the nose. The nasal sinuses were infected, and flare-ups of this infection were said to have an unfavorable effect on the skin lesions. Arsenical treatment had been effective, but when it was stopped new lesions appeared.

DISCUSSION

DR. WILE: I agree with the diagnosis. Those lesions which have disappeared have left no scars.

MYCOSIS FUNGOIDES. Presented by DR. JAMIESON.

A. Z., a Pole, aged 35, a laborer, had first noticed the appearance of small, pruritic, erythematous papules, about the size of a pinhead, on the ankles two months previously. Scattered over the arms, legs, flanks, abdomen and lumbar region were many single and confluent large erythematous plaques, superficially excoriated in places.

DISCUSSION

DR. WILE: I agree with the diagnosis of mycosis fungoides in an early stage.

A CASE FOR DIAGNOSIS. Presented by DR. JAMIESON.

P. M., aged 58, married, a molder, had first noticed a swelling of the forearms three and one-half years previously. An intensely pruritic erythematous papular eruption had then appeared, becoming generalized and persisting within a year. The skin was diffusely thickened, dry and scaly, with numerous small erythematous papules and many excoriations.

DISCUSSION

DR. WILE: I would consider this a case of lichenoid parapsoriasis.

A CASE FOR DIAGNOSIS. Presented by DR. UDO J. WILE and DR. HARTHER L. KEIM.

In a boy, aged 9 years, a scaly superficial ringed patch had appeared on the right arm ten months previously. It had rapidly disappeared, but had been followed by a constant succession of similar lesions on the trunk and extremities, with slight pruritus. A deep-seated vesicular and pustular eruption had then appeared on the hands and feet, with some edema. The lesions on the trunk varied from the size of a small coin to that of a small palm, and had at first been extremely superficial, mildly inflammatory, and with a tendency to central clearing. At the time of presentation they had become slightly infiltrated and were sharply demarcated, with little tendency to central clearing, while the eruption on the hands and feet had almost disappeared. No biopsy had been made.

DISCUSSION

DR. WILE: When this patient first came under our observation, a tentative diagnosis of dermatomycosis was made, but we were unable to demonstrate the presence of the parasite. There was some improvement under local antiseptic applications. The condition now resembles early granuloma fungoides.

DR. VARNEY: This case impresses me as one of early mycosis fungoides, with a coexisting dermatophytosis of the hands and feet.

DR. BARTHOLOMEW: The possibility of a drug eruption must also be considered in this case.

DR. WILE: This may be a drug eruption. I have never seen mycosis fungoides in so young a patient.

Index to Current Literature

DERMATOLOGY

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